Pediatrics

VOLUME 5 MARCH 1950 NUMBER 3

ORIGINAL ARTICLES

SUBDURAL FLUID AS A CONSEQUENCE OF PNEUMOENCEPHALOGRAPHY

By HONOR V. SMITH, M.D.,* AND BRONSON CROTHERS, M.D.
London and Boston

PNEUMOENCEPHALOGRAPHY has proved so useful in the investigation of disease of the central nervous system that it is now widely practised. It is therefore important that its inherent dangers should be clearly defined. When employed in the field of neurosurgery it may carry considerable risk, but as the information it affords is often invaluable the procedure is justified. But pneumoencephalography has also furthered the study of nonprogressive disease of the nervous system and has helped to elucidate some of the late effects of trauma, ischaemia and infection. It has therefore found a place in the management of such common neurologic disorders of childhood as cerebral palsy, epilepsy and feeblemindedness. In such conditions, however, the information gained is seldom indispensable and the procedure can therefore only be justified after its dangers have been carefully assessed.

In this department, several hundred children suffering from cerebral palsy, epilepsy and feeblemindedness are seen yearly and many of them are subjected to lumbar or cisternal pneumoencephalography. The indications for the procedure, the technic used, and the reactions most commonly seen have been described elsewhere.[1] It was shown that the information gained often helped to establish the anatomic diagnosis and thus facilitated both prognosis and management. Further experience has confirmed the value of pneumoencephalography in such cases and has shown that, provided the child's general condition is reasonably good, there is no progressive disease and that the hydrodynamics of the cerebro-spinal fluid are normal, the procedure is on the whole well tolerated and the mortality is negligible.

However, as experience has accumulated, it has been realized that in at least one third

From the Department of Pediatrics, Harvard Medical School, and the Pediatric Division of the Children's Medical Center, Boston, Mass.

Read at the American Neurological Society Meeting, Atlantic City, N.J., June 14, 1949.
(Received for publication Sept. 12, 1949.)

* Rockefeller Fellow from the Department of Neurology and Surgery, Radcliffe Infirmary, Oxford, England.

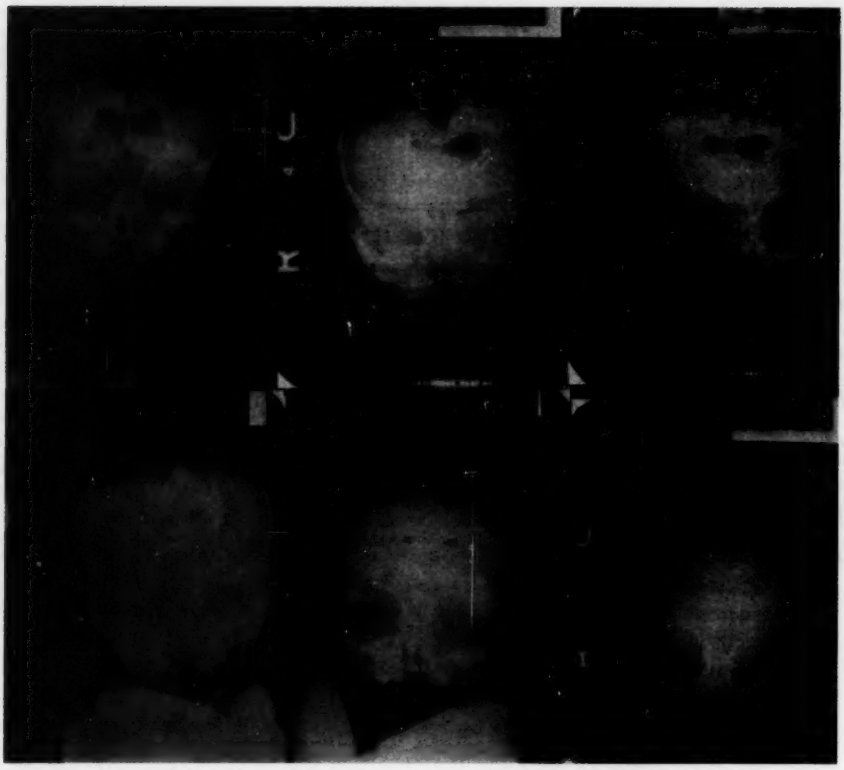


FIG. 1. Serial roentgenograms of case in which considerable amount of air entered subdural space during pneumoencephalography. Fluid level can be seen which rises as air is absorbed.

of cases air enters the subdural space, either alone or, more frequently, as well as the subarachnoid space and ventricles. In some of these cases subsequent roentgenograms showed that as the air was absorbed a definite fluid level appeared (fig. 1). At first no concern was felt over this but as time has gone on it has been found that in such cases the children often take longer than usual to recover from pneumoencephalography and may even become very ill. This experience agrees with that of Lemere and Barnacle.[2] They analysed a series of 800 pneumoencephalograms and found that not only did air commonly enter the subdural space but that in such cases the postoperative reaction was twice as severe as in the rest and the mortality three times as great.

In the present study, therefore, an attempt has been made to determine whether or not a definite syndrome is associated with the entry of air into the subdural space, and, if so, what is its nature and etiology.

ROENTGENOGRAPHIC DIAGNOSIS OF AIR IN THE SUBDURAL SPACE

The roentgenographic appearances of air in the subdural space, and the differentiation from subarachnoid air, have frequently been described.[2-6] The fact that the air really does lie in the subdural space has been confirmed both at operation by Cramer[7] and at

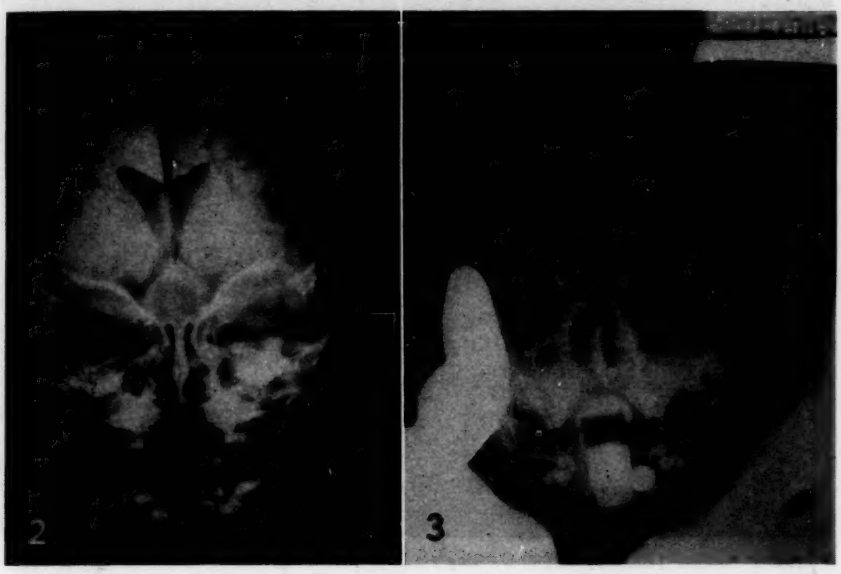


FIG. 2. Pneumoencephalogram showing air in subdural space. On axial projection taken in upright position, superior sagittal sinus is defined by air as it lies over hemispheres and dips down beside falx. More subdural air is on L than R and R lateral ventricle is somewhat depressed.

FIG. 3. Projections similar to Figs. 1 and 2. Although only small bubble of air is in subdural space on L, characteristic smooth border is shown as it lies beside superior sagittal sinus and falx which enables it to be correctly localized.

necropsy by Lemere and Barnacle.[2] Subdural air is best recognized on an axial projection taken in the upright position. The air is then seen lying over the cerebral hemispheres and dipping down beside the falx cerebri to outline the superior sagittal sinus (fig. 2). The smooth medial border of this air shadow and the consequent clear definition of the sinus is pathognomonic of subdural air and enables even small bubbles to be correctly localized (fig. 3). The presence or absence of the convolutional pattern is a less dependable sign because if air has entered both the subdural and subarachnoid spaces, the convolutional pattern will be visible though the characteristic cobweb pattern seen when only the subarachnoid space is filled is coarsened and distorted by the overlying subdural air (fig. 4). In addition to the air over the cerebral hemispheres, some is often trapped beneath the tentorium where it throws a characteristic triangular shadow.

It is perhaps worth emphasizing once again how important it is not to mistake the roentgenographic appearances of subdural air for those of cerebral atrophy or hypoplasia. In spite of the excellent descriptions in the literature this is often done and the mistake may only be corrected when subsequent pneumoencephalography shows that the subarachnoid space is perfectly normal (fig. 5). When much air has entered the subdural space it is usually impossible to assess the capacity and pattern of the subarachnoid space correctly. In such cases it is safer therefore to estimate the bulk of the brain from the size of the ventricles. Air in the subdural space tends to compress and displace the homolateral ventricle (figs. 2 and 6). If, therefore, the ventricles are still enlarged, it is good evidence that the size of the brain is, in fact, diminished.

FIG. 4. A. PEG (lateral), Case 3, showing air in both subdural and subarachnoid spaces. Consequent distortion of convolutional pattern can be misinterpreted easily as evidence of cerebral atrophy unless presence and significance of subdural air is appreciated. B. Axial projection in upright position. Considerable amount of air has entered subdural space. In spite of this, ventricles are enlarged showing that bulk of brain is diminished (*hydrocephalus a vacuo*).

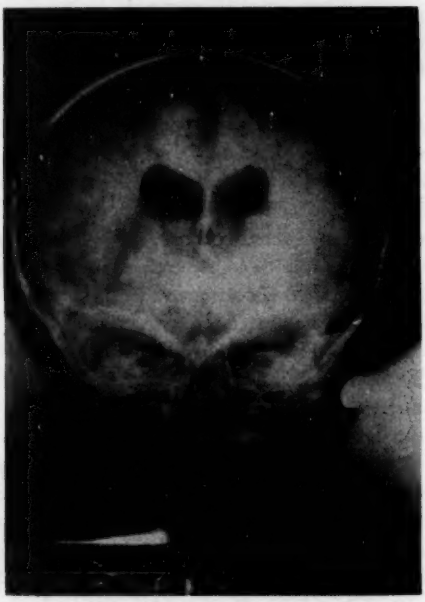


FIG. 5. Subsequent PEG, Case 3. No air has entered subdural space and convolutional pattern is in fact normal. Contrast with Figs. 4A lateral and 4B upright axial.

FIG. 6. PEG in proved case of Schilder's disease illustrating fallacy of interpreting these appearances as evidence of cortical atrophy. A. lateral; B. upright axial.

The term "cortical atrophy" when used in the interpretation of PEGs is really a misnomer. The site of the atrophic process cannot be localized from the roentgenograms and all that can justifiably be said is that the brain is smaller than it should be. For example, the PEGs in the proved case of Schilder's disease showed exactly the appearances often interpreted as typical of cortical atrophy; yet in Schilder's disease the brunt of the disease process falls on the central white matter of the cerebral hemispheres and not on the cortex (fig. 7).

It has been suggested that the entry of air into the subdural space indicates a pre-existing subdural hematoma.[8] Unless the air is clearly encysted or outlines a definite mass,[9] or

FIG. 7. PEG, Case 2, showing large amount of subdural air and consequent ventricular depression.

casts the characteristic finger-like shadow described by Dyke,[10] there is no evidence that this is so. The roentgenographic appearances are not those which have been seen in proved cases of subdural hematoma in children by Ingraham and Matson[11] or in adults by Van der Zwan.[12] Moreover, in many of the children in this series in whom large subdural air shadows were seen the subdural space had been tapped prior to pneumoencephalography with negative results. Indeed, so far from subdural air indicating subdural hematoma, the fact that it is possible, by altering the position of the head, to delineate almost the whole of the cerebral subdural space virtually precludes the presence of a hematoma.

Ingress of Air into Subdural Space

The most generally accepted explanation of how air introduced at lumbar or cisternal puncture enters the subdural space is that it is due to an error in technic. The needle may be accidentally misplaced so that its bevel is partly covered by the arachnoid membrane which then acts as a valve. Cerebro-spinal fluid can flow out through the needle but when, during the injection, the direction of flow is reversed the air enters, not the subarachnoid, but the spinal subdural space whence it passes upward over the cerebral hemispheres. That air can actually be introduced by this mechanism has been shown in the cadaver by Stone and Jones[13] and in life by Von Storch and Buermann.[4] The latter authors also discuss an alternative mechanism and suggest that air may sometimes pass directly from the subarachnoid to the subdural space through tears in the arachnoid membrane. They believe that this is the mechanism commonly involved when air which was seen immediately after injection to lie in the subarachnoid space appears 24 hours later in the subdural space.

The present study is concerned only with those cases in which air entered the subdural space during the actual procedure. Howard[14] showed in adults that after 30 to 50 cc. of cerebro-spinal fluid had been withdrawn with the patient in the sitting position, a negative pressure was set up in the subdural space. If burr holes were then made and the dura incised, air could be heard to enter the subdural space with a hiss and the brain would fall away from the skull and dura, leaving the subdural space widely patent. This helps to explain the ease with which air enters the subdural space during the lumbar pneumoencephalography; the low pressure presumably tends to suck air up into the subdural space unless the bevel of the needle lies wholely in the arachnoid space. But that this is the mechanism by which air commonly reaches the subdural space is by no means precluding the possibility that rents in the arachnoid play a part, and Howard points out how easily the abrupt falling away of the brain may tear the pacchionian granulations, or the arachnoid sheaths and vessels as they cross the subdural space to reach the superior sagittal sinus. This point will be referred to again.

Symptoms Associated with Subdural Air

Some reaction after lumbar or cisternal pneumoencephalography is the rule.[1] The children are pale, drowsy and feverish, and many vomit. If epilepsy has been a feature of their illness they may have fits either during or immediately after the procedure. Signs of mild meningeal irritation are also common. These symptoms are, however, short lived and typically subside within 12 to 36 hours.

In a proportion of the children in whom a considerable amount of air had entered the subdural space the clinical course was different. The symptoms which immediately fol-

lowed pneumoencephalography were the same but these either did not subside, or, if they did so, would reappear towards the end of the second or third, or even as late as the fifth postoperative day, and might then persist for well over a week. During this time the children were pale and drowsy and if aroused were intensely irritable. Projectile vomiting was the rule and was sometimes extremely troublesome, while occasionally the fontanelle became tense. In the following case pneumoencephalography was performed twice and both types of postoperative course exemplified.

Case 1 (CH 327263): Microcephaly: subdural air and fluid following lumbar pneumoencephalography. A boy 10 mo. of age was admitted to the neurologic ward of the Children's Hospital, Boston. He had been born at full term after a normal pregnancy and though the labor had been dry no instruments were used. He was cyanosed at birth and respiration was so delayed and so hard to establish that he was given continuous oxygen and kept in a respirator for the 1st 10 days of life.

When he was between 2 and 3 mo. old, his mother noticed that his head seemed smaller than normal and the disproportion between head and body became more obvious as he grew. He did not lift his head until he was 5 mo. old and feeding became progressively more difficult.

On admission the patient looked physically well. Mentally, however, he was grossly retarded and was unable to sit alone or turn himself over. Skull was small with severe occipital flattening; the sutures were prominent and the fontanelles almost closed. There were no other abnormal physical signs.

Lumbar PEG was performed under general anesthesia; 100 cc. of CSF were removed and replaced by 90 cc. of warmed and filtered air. Subsequent roentgenograms showed that apparently all the air had entered the subdural space and none was seen in the ventricles.

He recovered promptly from the anesthetic and for the next 48 hrs. convalescence was uneventful. He then began to vomit frequently and forcefully. This was interpreted as a sign of raised intracranial pressure due possibly to fluid as well as air collecting in the subdural space (fig. 1). Accordingly, the subdural space was needled through the coronal suture[11] and 8 cc. of xanthochromic fluid obtained from either side. During this procedure a little air was seen to bubble out through the needle. Analysis showed that the fluid contained over 400 mg./100 cc. protein and 800 to 900 fresh erythrocytes/cmm.

In spite of this procedure, vomiting grew worse; child refused to eat and became so dehydrated that frequent clyses were required. For the next 2 wks. the subdural space was tapped nearly every day and from 6 to 19 cc. of grossly bloodstained fluid containing protein 400 mg./100 cc. or more usually obtained. On this treatment the child gradually improved and by the end of the 2nd wk. had apparently recovered. He was alert, was taking his feedings well and was no longer vomiting.

Nineteen days after the 1st PEG, the procedure was repeated using the cisternal route; 22 cc. of CSF were removed and replaced by 25 cc. of air. On this occasion all the air entered the ventricles and none was seen over the hemispheres. Immediately after the procedure he was pale and somewhat collapsed; temperature was subnormal and breathing and pulse were slow. Three hours later, however, these signs had disappeared. From then on his course was uneventful and he was discharged 4 days later in the same condition as on admission.

Comment: In this case a large amount of air was introduced into the subdural space during lumbar PEG. This was followed 2 days later by symptoms suggestive of a high intracranial pressure and by the repeated recovery of large amounts of xanthochromic or bloodstained fluid with a high protein content from the subdural space. The speed and ease with which the child recovered from the 2nd PEG contrasts strongly with the long and stormy course which followed the first.

In this and similar cases the question arises of whether the symptoms are due simply to the pressure of air in the subdural space or whether some other factor is implicated. The air might expand, actively compressing the brain[7] and raising the intracranial pressure. There is evidence that this is not the mechanism involved. In a few children in whom a large quantity of subdural air was seen, the subdural space was needled immediately after the roentgenograms had been taken. A little air might bubble out when the child was raised into the sitting position, but this was clearly not under pressure and

subsequent roentgenograms showed that the brain was still "collapsed." Moreover, this procedure did not safeguard the child from a stormy postoperative course.

An alternative possibility is that air in the subdural space is irritating to the meninges and thus causes both the vomiting and the outpouring of fluid. A series of cases in which pneumoencephalography was performed was therefore reviewed in order to determine the frequency with which air entered the subdural space, how often this was followed by prolonged postoperative symptoms, whether the age of the patient was significant and, in particular, whether the production of the symptoms could be correlated with any other factor.

Frequency and Age Incidence of Subdural Air

As the case material accumulated in the records of this department is now considerable, this study was limited to children admitted to the neurologic ward during the first six months of 1948. This material is almost certainly representative of that seen in this

TABLE I

	Total	No. Showing Subdural Air	% Showing Subdural Air
Lumbar encephalograms	80	31	38%
Cisternal encephalograms	7	1	14%
Total	87	32	37%

department over several years. During the period of six months 75 children, of whom the great majority suffered from cerebral palsy, epilepsy or feeblemindedness in various combinations, were submitted to pneumoencephalography by either the lumbar or cisternal route. All PEGs were performed under general anesthesia, with the patient in the sitting position.[1] In several cases pneumoencephalography was performed more than once making a total of 87 PEGs. Those cases in which air was introduced directly into the ventricles were excluded from this study.

Using the criteria of diagnosis already described (*vide supra*, p. 378) subdural air was recognized in 32 (37%) of the 87 PEGs (Table I). As the use of the cisternal route may possibly introduce a complicating factor, the remainder of the analysis is confined to those 80 PEGs performed by the lumbar route.

Of the patients in this series roughly half were under 2 years of age whereas no less than 27 (73%) of the 31 PEGs showing subdural air were obtained in the younger age group. Conversely, air entered the subdural space in over two thirds of the children who were 2 years old or under (Table II).

This high incidence of subdural air in infants may account for the fact that the frequency of subdural air in this series is considerably higher than that reported by Lemere and Barnacle[2] who found subdural air in 20% of their series of 800 patients, with an average age of 32 years.

Relation of Symptoms to Subdural Air

In 11 of the 31 cases in which subdural air was seen, the postoperative course was disturbed. The symptoms were seldom as severe as those described in Case 1, but they

TABLE II

Age of Patient	1 to 12 mo.	13 to 18 mo.	19 to 24 mo.	Total 2 yr. and Under	Over 2 yr.	Total
No. encephalograms	16	14	7	37	43	80
No. showing subdural air	11	11	5	27	4	31

were always more persistent than those commonly occurring after pneumoencephalography and their onset was typically delayed. This particular syndrome was therefore relatively common and was seen in approximately 14% of the whole series. On the other hand, the fact that only about one third of the PEGs showing subdural air caused these symptoms strongly suggests that some factor other than the presence of air is involved. Further, if the symptoms were solely due to irritation by the air it is difficult to understand why their onset should be delayed.

TABLE III

	No. Cases	Post-op. Subdural Taps	Fluid Obtained
Subdural air without symptoms	20	5	1
Subdural air with symptoms	11	6	6

Another possibility is that it is the fluid rather than the air itself which is the cause of the symptoms. In several children in whom a large amount of subdural air was seen, the subdural space was needled within a few days of the procedure, whether or not they had symptoms at the time. The results are shown in Table III.

TABLE IV

	No. Cases	Ventricles Normal	Ventricles Dilated
Subdural air without symptoms	20	14	6
Subdural air with symptoms	11	4	7

In only one of the five cases without symptoms was fluid obtained. In this case 2 cc. of clear colorless fluid were obtained; since the protein count was low (33 mg./100 cc.), it was probably CSF. By contrast, of the six cases in which the postoperative syndrome associated with subdural air was seen, fluid was obtained in every case. In one of these also, the fluid, as judged by its appearances and protein content, was probably CSF but in the others the fluid had a high protein content, sometimes as high as 400 to 1000 mg./100 cc. and was typically bloodstained or xanthochromic.

There was no evident relation between the occurrence of symptoms and the amount of subdural air seen on the roentgenogram. There was, however, a strong suggestion that symptoms were commoner in those patients in whom the lateral ventricles were greatly

enlarged than in those in whom they were either normal or only slightly dilated.* (See Table IV).

Nature of the Subdural Fluid

The evidence thus suggests that the symptoms which sometimes occur after air has been introduced into the subdural space are related to the presence of subdural fluid rather than to the presence of air itself.

The composition of this fluid varied from case to case. Occasionally it was clear and either colorless or pale yellow and with a low protein content and was thus probably CSF with or without a slight admixture of blood. As a rule, however, it was indistinguishable from that found in subdural hematomata in children.[11] Moreover, the syndrome under discussion, namely drowsiness and irritability, fits, vomiting, reluctance to feed and, occasionally, overt signs of increased intracranial pressure, is entirely compatible with a diagnosis of subdural hematoma.

That some of the collections of fluid seen after pneumoencephalography were, in fact, indistinguishable from subdural hematomata is demonstrated by the following two cases.

Case 2 (CH 334500): Mental deficiency; negative bilateral subdural exploration by needling; pneumoencephalography; subdural hematoma.

Patient, a boy 9 mo. of age, was born at full term after a normal pregnancy. Delivery and neonatal period were uneventful and he seemed well until 4 mo. of age when he began to have frequent fits. These were generalized and continued until the time of admission.

On admission his general condition was good but mentally he was seriously retarded. He took no interest in surroundings and was unable even to lift his head or to follow a light with his eyes. All tendon reflexes were a little brisk but there were no abnormal physical signs. Anterior fontanelle was open and slack. Roentgenographic examination of his head showed that the anterior fossa was abnormally shallow and EEG showed generalized seizure discharge patterns.

Subdural space was needled bilaterally but no fluid was obtained. Pneumoencephalogram was then done; 100 cc. of CSF was withdrawn by lumbar puncture and replaced with air. Subsequent roentgenograms showed symmetric dilatation of the lateral ventricles and good filling of the basal cisterns. There was a small amount of subdural air on the left side and a large amount on the right with consequent depression of the right lateral ventricle (fig. 6.) In none of the views was there any indication of a subdural collection of fluid.

Following the procedure patient vomited frequently and on the 3rd postoperative day bilateral subdural taps were performed and 10 cc. of dark orange fluid obtained from the right side. This fluid contained 675 mg./100 cc. protein and was loaded with fresh and crenated erythrocytes.

Subdural taps were repeated daily for the next 10 days with similar results. Protein content of the fluid slowly increased to 1.73 gm./100 cc., and 2 wks. after the PEG bilateral burr holes were made. On the right, the side on which the large amount of subdural air was seen and from which the large amount of bloodstained fluid was first obtained, a subdural hematoma was found and evacuated. Seven days later a right craniotomy was performed and a subdural membrane was excised. The child's recovery was uneventful and he was discharged after being in the hospital for 5 wks.

Comment: This child had a subdural hematoma which was confirmed at operation and the evidence is that it followed rather than preceded the PEG since the subdural taps done on admission were dry, the roentgenographic appearances on pneumoencephalography showed nothing to suggest a pre-existing subdural hematoma, while the subdural fluid obtained subsequently showed unequivocal evidence of recent bleeding.

In the second case the evidence that the subdural hematoma followed rather than pre-

* The total number of cases considered here is small but if this sample is representative of the whole, as it probably is, then the difference between the frequency of symptoms among those patients in whom the ventricles were enlarged and those in whom they were not is statistically significant.

ceded the PEG and was responsible for the postoperative symptoms is even more conclusive.

Case 3 (CH 285136): Mental deficiency; epilepsy; subdural hematoma PEG.

The patient was first admitted to the Children's Hospital when he was 7 mo. old. Pregnancy, labor and neonatal period were uneventful but he had always been listless and apathetic and when he was about 2 wks. old vomited once or twice a day. The vomiting stopped after 3 wks. but although he thrived well he was always unresponsive to his surroundings and never learned to roll over or hold up his head. When he was 5½ mo. old he began to have fits. These were generalized and recurred 4 to 6 times daily up to the time of admission to the hospital.

On examination the patient looked well but his mental development was grossly retarded. He took no interest in surroundings and was unable to sit or roll over. Muscles of limbs and trunk were hypotonic but no localized weakness could be demonstrated. Head was normal in size, sutures were not separated and fontanelle was open and soft. He had frequent fits which consisted of generalized tonic seizures ushered in by a cry.

Lumbar punctures yielded fluid under pressure containing no cells and protein 20 mg./100 cc. Bilateral subdural taps yielded 2 cc. of faintly bloodstained fluid from each side. As this contained only 32 mg./100 cc. protein it was thought to be CSF. In order to confirm this both lumbar puncture and the subdural taps were repeated a week later. The lumbar CSF contained protein 36 mg./100 cc. and no fluid could be obtained from the subdural space.

Lumbar PEG was then performed; 105 cc. of CSF were withdrawn and replaced by an equal quantity of air. Subsequent roentgenograms showed a considerable quantity of subdural air especially on the right side. Ventricles were filled and were symmetrically dilated (fig. 4). A full series of roentgenograms with the head in different positions showed no evidence of fluid or solid subdural hematoma.

Immediate recovery was uneventful but 3 days later he began to have repeated severe projectile vomiting and the fontanelle was seen to be bulging. Several decompressive lumbar punctures were done but in spite of this the fontanelle remained tense and during the next week circumference of the head increased by 2.5 cm.

Eight days after PEG bilateral subdural taps were performed and yellow fluid containing protein 6 gm./100 cc. was obtained on each side. One week later bilateral burr holes were made; bilateral subdural hematoma were found and evacuated. Some weeks later first a right and then a left osteoplastic flap was turned; bilateral subdural membranes were found and excised and their identity confirmed by histologic examination. Postoperative course was disturbed by a mild infection of one wound. This was controlled by chemotherapy and the patient was discharged after spending 60 days in the hospital.

During the next 3½ yr. the patient was seen regularly in the outpatient department. General health remained good and convulsions ceased but mentally his development was extremely slow and he did not learn to sit until he was 4 yr. of age. When he was just over 4 yr. old he was taken into the hospital in order to exclude the presence of any harmful residue from his hematomata.

On examination at this time he was rather small for his age but showed no other abnormal physical signs. Mentally, however, he was grossly retarded; he would spend hours beating his hands together and knocking his head but beyond crying lustily whenever he was examined he took no notice of surroundings. He was unable to talk, stand or crawl, and constantly soiled or wet himself.

A 2nd lumbar PEG was performed. This time all the air entered the subarachnoid space and ventricles (fig. 5). Symmetric ventricular dilatation recognized on the first encephalogram had increased a little but the whole of the subarachnoid space was well delineated and was normal. The postoperative course was entirely smooth.

The child was last seen when he was 4½ yr. old and was still grossly defective mentally.

Comment: In this case also the diagnosis of subdural hematomata was confirmed by operation and by histologic examination of the subdural membranes. That these hematomata predated the PEG is highly unlikely in view of the 2 negative subdural taps done before the 1st PEG, and of the roentgenographic findings. In this case the signs of raised intracranial pressure, appearing 3 days after the PEG, were unequivocal.

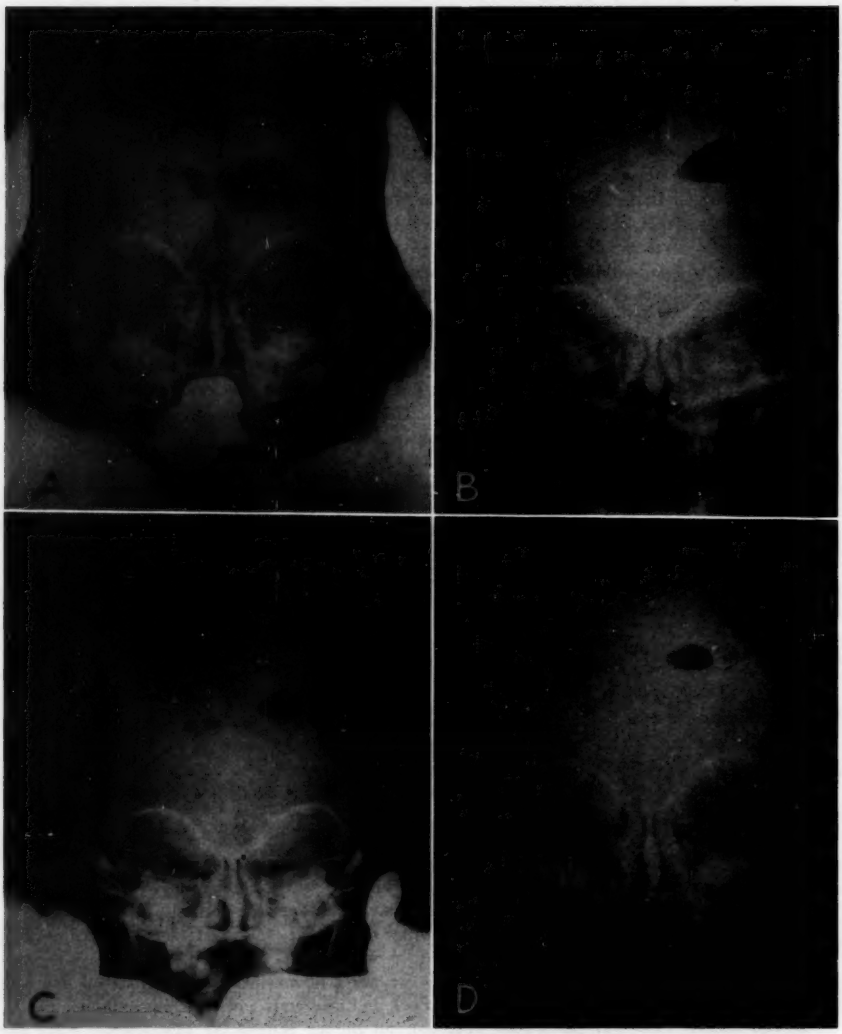


FIG. 8. Serial PEGs (upright axial) in child suffering from mental deficiency and hemiplegia. Fig. 8A shows large amount of subdural air. Vessels in their arachnoid sheaths can be clearly seen as they cross subdural space and appear to be under considerable tension. Fluid level can already be made out. Subdural space was tapped few hours later and about 15 cc. intensely bloodstained fluid obtained. On microscopy, blood appeared fresh. Figs. 8B, C and D, taken on successive days, show gradual absorption of air and rising fluid level. Subdural space was needled daily and fluid seen to undergo same changes as in traumatic subdural hematoma of infants. As fluid was removed, large porencephalic cyst became visible.

Discussion

It is important to know whether these hematomata pre-exist or result from the PEG. The evidence is all in favor of the hypothesis that the hematoma results from the entrance of air into the subdural space during pneumoencephalography. Firstly, in several of the cases (e.g., Cases 1 and 2) subdural taps were performed before the air was injected and were negative, while they yielded abundant fluid after pneumoencephalography. Secondly, when the subdural fluid was obtained within the first two or three days of the air injection, it was typically not only heavily bloodstained but the blood was quite fresh. As time went on the erythrocytes became crenated and then disappeared leaving an almost transparent dark red or orange fluid with a high protein content. Thirdly, although the hematomata were thus apparently recent, their removal was of immediate benefit only and in no case did the child's fundamental disability improve, suggesting that the subdural hematoma had not produced the symptoms which brought the child to the hospital. Finally, the PEGs themselves were in no way similar to those seen in proved cases of subdural hematoma (*vide supra,* p. 381).

It is not difficult to understand how subdural bleeding could set up during pneumoencephalography. Since Trotter's[15] classical paper on subdural hematoma, it has been generally accepted that "it is nearly certain that the cerebral veins passing from the brain to the superior longitudinal sinus are always the source of the blood." When air enters the subdural space and the brain falls away, as described by Howard,[14] these vessels with their sheaths of arachnoid must be severely stretched and strained (fig. 8). Should these vessels tear then blood will accumulate in the subdural space where it will undergo the same changes and produce the same effects as do the traumatic subdural hematomata described by Ingraham and Matson.[11] Similarly, if the sheaths of the vessels or the pacchionian granulations should tear, then CSF will be liberated into the subdural space. Howard,[14] who introduced air directly into the subdural space at operation, found that fluid might subsequently collect. He believed that this was CSF which escaped from the subarachnoid space through rents in the arachnoid. This might explain why the fluid obtained on needling the subdural space soon after pneumoencephalography, though heavily contaminated with fresh blood, was yet not undiluted blood (fig. 8). Nor was a solid hematoma ever encountered, possibly because the dilution of blood by CSF was sufficient to prevent clotting. The same mechanism may well be involved in those occasional cases in which the subdural fluid was found to be colorless or faintly yellow or to have a low protein content.

The frequency with which the symptoms associated with subdural collections of blood occurred in childen with severe cerebral hypoplasia or atrophy (Table IV) is interesting. Subdural hematoma of adults is commonest in later life and is especially associated with diseases which tend to cause atrophic conditions of the brain.[15] Further, studies of etiology of subdural hematoma of adults shows that although trauma is certainly a factor, there are many cases in which either no history of injury can be obtained or in which the injury was trivial.[12] By analogy, therefore, with our cases, it is possible that a fall in intracranial pressure in those in whom the bulk of the brain is diminished may be a factor of etiologic importance.[16]

Conclusions

It may be concluded therefore that when lumbar pneumoencephalography is performed on infants air may enter the subdural space; nor have we been able to prevent this by

using the cisternal route instead of the lumbar. The entry of air allows the brain to fall away from the dura and thus stretches those structures which cross the subdural space. In about one third of cases these structures apparently tear, blood and CSF collect in the subdural space, and a subdural hematoma may result. This risk would seem to be much greater in infants than in the older age groups, and is possibly greater in those children in whom the brain is atrophic or hypoplastic and the ventricles consequently enlarged than in those in whom the brain is of normal size. The results of such an accident are apparently seldom, if ever, severe enough to endanger life and once the situation is appreciated they can be dealt with relatively easily. They may, however, greatly increase the time the child must remain in the hospital and occasionally operation becomes necessary. The fact that a subdural hematoma is found after pneumoencephalography in a child with cerebral palsy or mental deficiency is no evidence that it is the cause of his disability nor that its removal will cure him.

Summary

When lumbar or cisternal pneumoencephalography is carried out on children with nonprogressive brain lesions causing mental deficiency, cerebral palsy or epilepsy, air is seen in the subdural space in at least a third of cases. This proportion is much larger in children 2 years of age or under.

The roentgenographic appearances of subdural air are described and the importance of not attributing these appearances to cerebral atrophy or hypoplasia is emphasized.

In approximately one third of cases in which air enters the subdural space, that is, in from 10% to 15% of all cases, recovery from pneumoencephalography is delayed by the development of signs and symptoms suggesting a rise in intracranial pressure.

In such cases fluid can usually be found by needling the subdural space. Typically this fluid is characteristic of that found in subdural hematoma. There is no evidence that such a collection of fluid was present before pneumoencephalography.

It is therefore suggested that as air enters the subdural space and the brain falls away from the dura, vessels may be torn as they cross this space to reach the superior longitudinal sinus, with the formation of what may be termed subdural hematoma artefacta.

Although the incidence of this complication is moderately high, its effects are seldom serious, provided the situation is appreciated and suitable treatment given. The length of time the child spends in the hospital is, however, often greatly prolonged and occasionally operation proves necessary for removal of a subdural membrane.

Since the subdural hematoma is an artefact occurring in the course of treatment, its removal does not influence the ultimate prognosis.

It is tentatively suggested that, by analogy with these cases, a fall in intracranial pressure in those in whom the bulk of the brain is diminished might be a factor in the etiology of subdural hematoma of adults.

References

1. Crothers, B., Vogt, E. C., and Eley, R. C., Encephalography in cases with fixed lesions of brain, Am. J. Dis. Child. **40**:227, 1930.
2. Lemere, F., and Barnacle, C. H., Encephalography: Review of 800 encephalograms with special reference to subdural air, Arch. Neurol. & Psychiat. **35**:990, 1936.
3. Pendergrass, E. P., Encephalography: Explanation of possible error in technique, Am. J. Roentgenol. **25**:754, 1931.

4. Von Storch, T. J. C., and Buermann, A., Subdural shadows in pneumoencephalograms, Arch. Neurol. & Psychiat. **42**:810, 1939.
5. Pancoast, H. K., Pendergrass, E. P., and Schaeffer, J. P., Head and Neck in Roentgen Diagnosis, Baltimore, Charles C Thomas, Publisher, 1942.
6. Schiller, F., Cairns, H., and Russell, D. S., Treatment of purulent pachymeningitis and subdural suppuration with special reference to penicillin, J. Neurol., Neurosurg. & Psychiat. **11**:143, 1948.
7. Cramer, F., Note on occurrence and significance of air in subdural space after encephalography, Bull. Neurol. Inst. New York **3**:506, 1934.
8. Holt, W. L., Jr., and Pearson, G. B., Chronic bilateral subdural hematoma: Encephalographic diagnosis with report of 3 cases, Arch. Neurol. & Psychiat. **37**:1161, 1937.
9. Von Storch, T. J. C., and Munro, D., Encephalography in diagnosis of subdural hematomas: Analysis of 35 cases, New England J. Med. **218**:6, 1938.
10. Dyke, C. G., Pathognomonic encephalographic sign of subdural hematoma, Bull. Neurol. Inst. New York **5**:135, 1936.
11. Ingraham, F. D., and Matson, D. D., Subdural hematoma in infancy, J. Pediat. **24**:1, 1944.
12. Van der Zwan, A., Chronic subdural hematoma, Folia Psychiat. Neurol. Neurochi. **51**:385, 1948.
13. Stone, R. S., and Jones, O. W., Jr., Encephalography: Review of 113 cases and report of post-mortem studies on injection of air, Radiology **21**:411, 1933.
14. Howard, C., Subdural pneumography, Am. J. Roentgenol. **55**:710, 1946.
15. Trotter, W., Chronic subdural haemorrhage of traumatic origin and its relation to pachymeningitis haemorrhagic interna, Brit. J. Surg. **2**:271, 1914.
16. Robertson, G. M., Formation of subdural membranes or pachymeningitis haemorrhagica, J. Ment. Sc. **39**:203 and 368, 1893.

SPANISH ABSTRACT

Fluído Subdural como una Consecuencia de Neumoencefalografía

Se reportan observaciones en 80 neumoencefalogramas consecutivos en niños que no tenían enfermedad neurológica aguda. En infantes menos de 2 años de edad, se encontró aire subdural en un 70%, mientras que en niños mayores de 2 años se encontró en 10%. En infantes, ocurrieron síntomas de pena en una tercera parte de los casos con aire, mientras que solamente una quinta parta de los niños mayores dieron muestra de pena.

La pena, en casi todos los casos, fué el resultado de la rápida acumulación de flúido amarillo o con manchas de sangre en el espacio subdural. Se obtuvo alivio inmediatomediante drenaje con agujas; pero en unos pocos casos fué necesario el drenaje operativo para evitar que se volviera a formar el flúido.

Se debrían de revisar las indicaciones para neumoencefalografía en infantes y se debría de poner más atención a la observación después de la operación.

300 Longwood Avenue

RIGHT HEART CATHETERIZATION OF THE AORTA THROUGH A PATENT DUCTUS ARTERIOSUS

Report of Two Cases

By FORREST H. ADAMS, M.D., JOHN LABREE, M.D.,
AND HERBERT M. STAUFFER, M.D.
Minneapolis

IN AN effort to demonstrate more conclusively the presence of a patent ductus arteriosus in patients in whom the diagnosis is not entirely obvious, right heart catherization, as described originally by Cournand and Ranges,[1] has been used by the authors. If the pulmonary valve and right ventricle are anatomically within normal limits, the pulmonary artery can usually be entered with the catheter, once it reaches the right ventricle. Elevation of the oxygen content of the blood in the pulmonary artery above that in the right ventricle indicates a shunt of blood from left to right such as occurs in a patent ductus arteriosus. Such data have already been presented and confirmed at surgery by others.[2,3] In two patients suspected of having a patent ductus arteriosus in whom the authors were manipulating the catheter through the main pulmonary artery in an attempt to advance it out into the "pulmonary capillary area," the catheter passed into the patent ductus arteriosus and down the aorta. No previous recorded instance of such an occurrence having been found, the cases are reported here in some detail.

CASE REPORTS

Case 1 (see fig. 1a-d).—S. B., a 4½ yr. old female, believed to have had congenital heart disease discovered for the first time at 14 mo. of age, was referred to the University Hospitals for further follow-up of her cardiac status. The mother said that the patient had progressed normally until 7 mo. of age when she seemed to be less active. Respiratory infections occurred more frequently and lasted longer than in her siblings. She was treated by one doctor for rickets without apparent improvement. At 14 mo. of age she was taken to another doctor who informed the mother that the child had congenital heart disease. She was hospitalized at 16 mo. of age for a severe respiratory infection at which time a cardiologist saw the patient in consultation and made a diagnosis of an interatrial septal defect. From then until she was seen at the University Hospitals, she was followed by her family doctor, who referred her with the diagnosis of interventricular septal defect. The mother volunteered that the child had been well in the intervening time and was active physically, limited only by shortness of breath on moderate exertion. There was no history of cyanosis. The birth history, developmental and family history were all noncontributory.

Physical examination revealed a poorly developed, poorly nourished female who was in no distress. Chest appeared to have a moderate pigeon-breast deformity with Harrison's grooves present. Apex beat of the heart was just beyond the nipple line in the L IV ICS. A thrill was palpable over the L II and III ICS and a loud rumbling murmur continuous through systole to early diastole was heard best in the L II and III ICS. Blood pressure in upper extremities was 105/58/0 mm. Hg. and in lower extremities was 130/52/0. ECG revealed a tendency to R axis deviation with high voltage of QRS complexes in all leads. Roentgenograms and fluoroscopic examination revealed enlargement of

From the Departments of Pediatrics, Medicine, and Roentgenology, University of Minnesota Medical School, Minneapolis, Minn.

Performed under a cooperative agreement between the University of Minnesota and the National Heart Institute of the U. S. Public Health Service, Bethesda, Md.

(Received for publication June 20, 1949.)

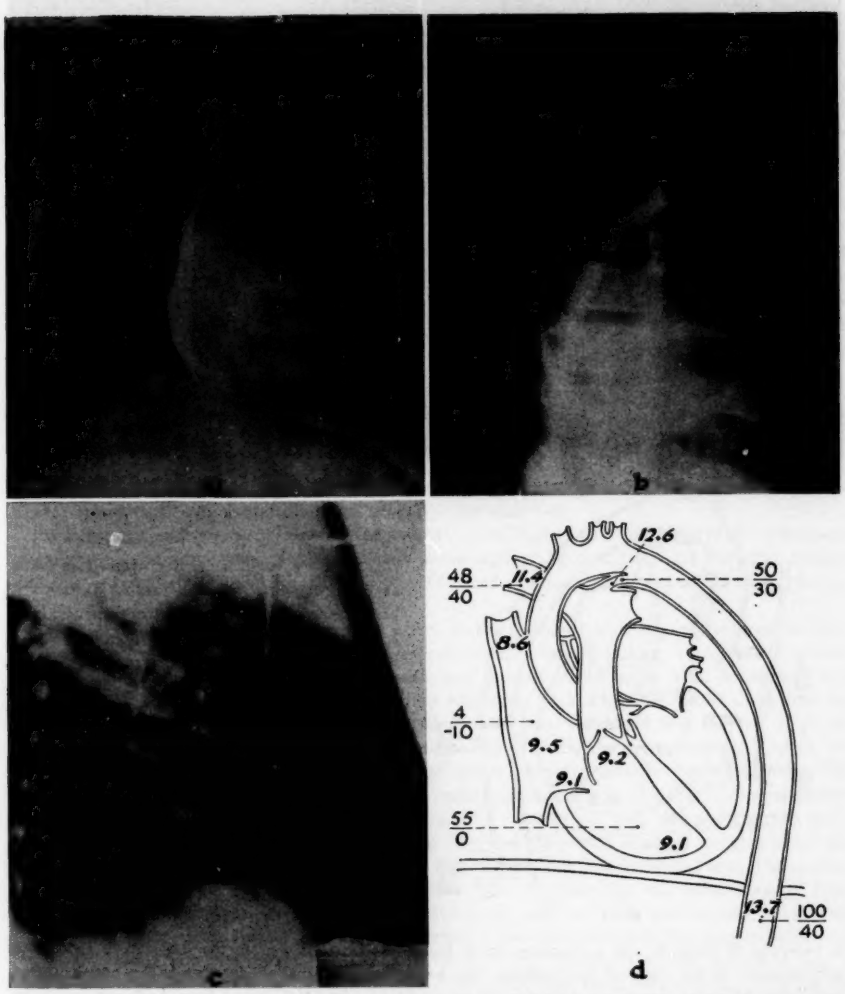


FIG. 1. Patient S. B. a. Roentgenogram taken at 6 ft. showing enlarged cardiac contour, prominent pulmonary vascular markings and deviation of barium-filled esophagus to right. b. Roentgenogram showing catheter passing through R heart, pulmonary artery, ductus arteriosus and R descending aorta. c. Roentgenogram taken in R lateral position confirming presence of catheter in descending aorta. d. Pictorial representation of heart and greater vessels to show data obtained from cardiac catheterization. Darker numerals represent oxygen content values in volumes per cent of blood removed from those areas. Lighter numbers represent systolic and diastolic pressures in areas indicated.

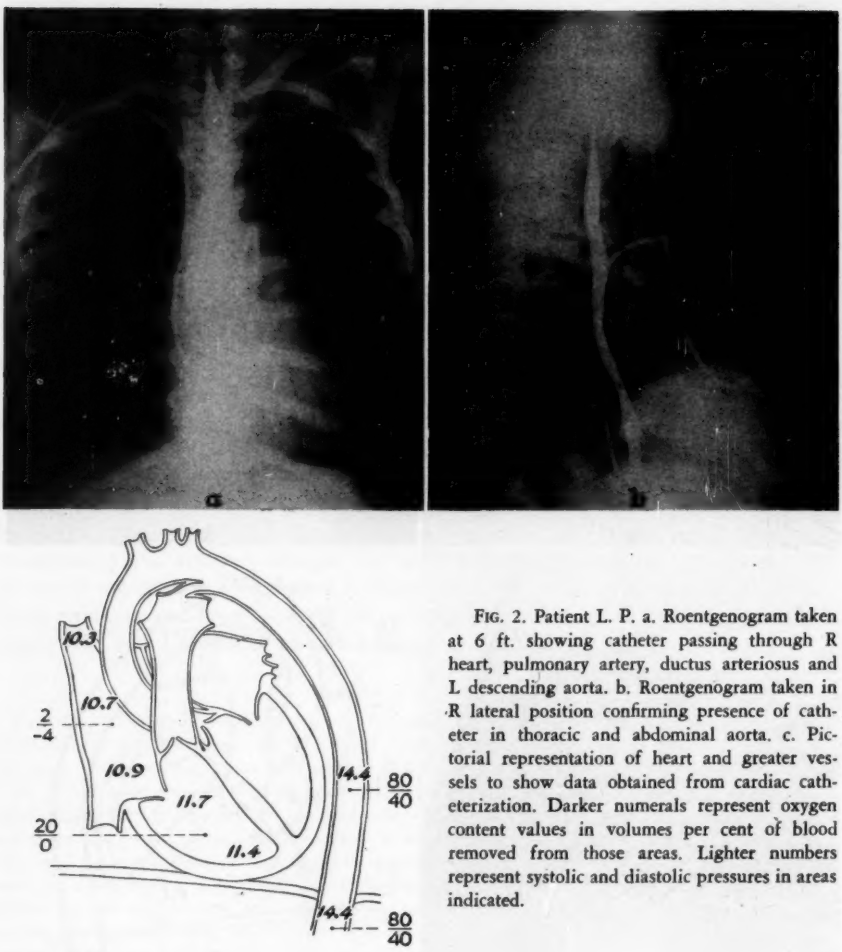


FIG. 2. Patient L. P. a. Roentgenogram taken at 6 ft. showing catheter passing through R heart, pulmonary artery, ductus arteriosus and L descending aorta. b. Roentgenogram taken in R lateral position confirming presence of catheter in thoracic and abdominal aorta. c. Pictorial representation of heart and greater vessels to show data obtained from cardiac catheterization. Darker numerals represent oxygen content values in volumes per cent of blood removed from those areas. Lighter numbers represent systolic and diastolic pressures in areas indicated.

L ventricle, R ventricle and pulmonary artery trunk. Aortic arch was on the left. Lower esophagus was deviated to the right of the midline. The impression was that the patient had a patent ductus arteriosus. However, because a diagnosis of an interatrial septal defect had been made previously by a cardiologist, and because the heart murmur was not entirely characteristic of a patent ductus arteriosus, the patient was admitted for cardiac catheterization.

Under basal rectal avertin anesthesia plus procaine locally, incision was made in L medial basilic vein and a No. 6 ureteral catheter was inserted. The catheter slipped easily into the axillary vein, but considerable difficulty was encountered in getting the catheter to go into the superior vena cava. After 8 minutes of fluoroscopy, the catheter finally entered the superior vena cava, R atrium, R ventricle and then the R pulmonary artery with ease. The pressure in the pulmonary artery was 55/48 mm.Hg., and oxygen content of the blood was 11.38 volumes per cent. The catheter was withdrawn in the region of the pulmonary conus and attempts to readvance the catheter out into the R pulmonary artery were unsuccessful. However, the catheter passed posteriorly, to the right and down. On further advancing the catheter, it definitely appeared to be in the abdominal aorta, undoubtedly passing through the patent ductus arteriosus. In this region the pressure was 110/55 mm.Hg. Oxygen

content of the blood was 13.69 volumes per cent. Several roentgenograms were exposed in the AP and lateral views, as shown in Figs. 1b and c, confirming the position of the catheter in the aorta. The descending aorta deviated to the right of the midline. Esophagrams with the catheter in the aorta demonstrated that the right-sided descending aorta was responsible for the deviation of the esophagus to the right. The catheter was withdrawn into the right ventricle where the pressure was 55/0 mm.Hg., and the oxygen content of the blood was 9.19 volumes per cent. The catheter was withdrawn into the right atrium where the pressure was 4/-10 mm.Hg., and the oxygen content of the blood was 9.45 volumes per cent. The catheter was further withdrawn into the superior vena cava where the oxygen content of the blood was 8.58 volumes per cent. A pictorial representation of these data is shown in Fig. 1d.

Since catheterization clearly demonstrated the presence of a patent ductus arteriosus, the patient was subjected to surgery, and the ductus arteriosus was ligated.

Case 2.—L. P., a 14 yr. old female, was referred to the University Hospitals for evaluation of her cardiac condition and abdominal pain. She was known to have had a cardiac abnormality since 2 mo. of age when she was first taken to the family physician because of failure to gain weight. She had always been small and underweight for her age and was unable to participate in normal vigorous activity without becoming easily exhausted. There had been no history of cyanosis. Her abdominal pain, located in the R upper quadrant, had been periodic for several years, apparently unrelated to diet or activity.

Physical examination revealed a small poorly developed female in no distress. The blood pressure was 134/60/20 mm.Hg. in the arms and 166/90 mm. in the legs. The chest appeared normal, and no definite thrill could be palpated. A loud systolic murmur could be heard over the entire precordium but best in the L II and III ICS. There was no definite diastolic murmur audible on the initial examination. No abnormalities were found in the abdomen.

Fluoroscopic and roentgenographic examination of the heart and chest revealed L ventricular enlargement with prominence of the pulmonary artery segment, increased vascular markings, marked hilar vascular pulsations and a L aortic arch. The ECG had a normal axis deviation and slight peaking of P_2 and P_3.

The impression was that the patient had patent ductus arteriosus with atypical findings. In order to confirm this, right heart catheterization was performed. Under morphine, hyoscine and seconal premedication, 1% procaine was infiltrated locally over the left medial basilic vein. A cut-down was made and a No. 8 ureteral catheter was inserted with ease. The catheter advanced easily into the heart and out into the L pulmonary artery. The catheter was withdrawn into the region of the pulmonary conus, and when attempts were made to advance it into the pulmonary artery again, the catheter turned posteriorly and passed through the ductus arteriosus into the descending aorta. The pressure in this region was 80/40 mm.Hg. Blood removed from one area revealed an oxygen content of 14.1 volumes per cent and from another region 14.4 volumes per cent. The catheter was withdrawn into the R ventricle where the pressure was 20/0 mm.Hg.; blood removed revealed an oxygen content of 11.4 volumes per cent in one area and 11.7 volumes per cent in another area. The catheter was withdrawn into the R auricle where the pressure was 2/-4 mm.Hg., and blood removed from one area revealed an oxygen content of 10.87 volumes per cent and from another area revealed an oxygen content of 10.74 volumes per cent. The catheter was withdrawn into the superior vena cava where the blood removed revealed an oxygen content of 10.3 volumes per cent. Figures 2a and b are roentgenograms taken with the catheter tip in the abdominal aorta showing the course of the catheter through the heart, patent ductus and the aorta. Figure 2c is a pictorial representation of the data obtained from the catheterization.

Since in this patient likewise the presence of a patent ductus arteriosus was clearly demonstrated, the thorax was explored. A moderate sized patent ductus was found and ligated.

Discussion

Unquestionably, right heart catheterization is of value in establishing the diagnosis of patent ductus arteriosus in patients in whom atypical findings are present. Only after such a procedure has shown its existence should such patients be subjected to surgical treatment. A later communication, it is hoped, will show the variations in findings of such patients with patent ductus arteriosus.

It is not certain what value there is in being able to catheterize the aorta through the ductus arteriosus other than proving the existence of a communication between the pulmonary artery and the aorta. As can be inferred from the roentgenograms taken during the procedure, it was possible to catheterize some of the branches of the aorta, including the renal artery. Such a feat might present a possibility for certain physiologic studies on the kidney.

Paul[4] has recently described two patients operated upon for cyanotic congenital heart disease, each of whom had a left aortic arch with a right decending aorta. Edwards[5] has described a patient at postmortem with a left aortic arch, right ligamentum arteriosum and right descending aorta resulting in a vascular ring. In discussing the surgical implications of such anomalies, Edwards states that usually the ductus arteriosus or ligamentum arteriosum lies on the same side of the body as is the aortic arch. In Case 1 previously described, there was a left aortic arch, and catheterization of the aorta demonstrated a right descending aorta. The esophagus in this patient remained to the right of the aorta in contrast to Paul's and Edwards' patients in whom the position of the lower thoracic aorta and the esophagus were reversed. This is of obvious importance to roentgenologists interpreting the position of the aorta from the barium-filled esophagus and also to the surgeons planning to ligate the ductus arteriosus in such a patient.

Summary

Two patients with atypical findings of a patent ductus arteriosus are presented in whom right heart catheterization proved its existence by the catheter passing through the ductus into the aorta.

Right heart catheterization in one of these patients demonstrated a right descending aorta in the presence of a left aortic arch, the fourth patient with this anomaly to be reported.

Addendum

Since this manuscript was submitted for publication, it has been possible, using the right heart catheterization technic, to pass a catheter through the ductus arteriosus into the aorta in another patient with slightly atypical findings of patent ductus arteriosus. This patient was a female 7 yr. of age who had been asymptomatic. Her heart murmur was discovered only on routine physical examination. She had a typical machinery-like murmur and a slight thrill over the pulmonary artery region. The blood pressure, however, was within normal limits and the ECG had R axis deviation. Because of these latter findings right heart catheterization was performed. After samples of blood were removed from both the R and L pulmonary artery it was purposefully attempted to pass the catheter through the ductus into the aorta; this was successful. Following demonstration of the presence of a patent ductus arteriosus by right heart catheterization, this patient was submitted to surgery; the ductus arteriosus was found and ligated.

References

1. Cournand, A., and Ranges, H. A., Catheterization of right auricle in man, Proc. Soc. Exper. Biol. & Med. **46**:462, 1941.
2. Dexter, L., and others, Studies of congenital heart disease, J. Clin. Investigation **26**:561, 1947.
3. Cournand, A., Baldwin, J. S., and Himmelstein, A., Cardiac catheterization in congenital heart disease, New York, Commonwealth Fund, 1949.
4. Paul, R. N., New anomaly of aorta: Left aortic arch with right descending aorta, J. Pediat. **32**: 19, 1948.

5. Edwards, J. E., Retro-esophageal segment of left aortic arch, right ligamentum arteriosum and right descending aorta causing congenital vascular ring about trachea and esophagus, Proc. Staff. Meet., Mayo Clin. **23**:108, 1948.

SPANISH ABSTRACT

Cateterismo Derecho del Corazón de la Aorta Mediante un Patente Ductus Arteriosus; Informe de Dos Casos

Se presentan dos pacientes con descubrimientos atípicos de un patente ductus arteriosus, en quienes el cateterismo de corazón derecho probó su existencia al pasar el catéter al través del conducto en la aorta.

El cateterismo derecho del corazón en uno de estos pacientes demostró una aorta derecha descendiente en la presencia de un arco aortíco izquierdo, se informará sobre el cuarto paciente con esta anomalía.

University of Minnesota Medical School

ELECTROCARDIOGRAM IN 679 HEALTHY INFANTS AND CHILDREN

By MARGARET MARONEY, M.D., AND LOWELL A. RANTZ, M.D.
San Francisco

IT HAS long been apparent that the conduction time of the cardiac impulse is shorter in children than in adults. There has been little information available in regard to the normal variations to be expected in the years from 1 to 9 when the size of the individual increases many times and the electrocardiographic measurements must also change. The present study was planned for the purpose of obtaining information necessary to fill this gap in essential clinical knowledge.

REVIEW OF THE LITERATURE

A review of the literature on the subject of electrocardiograms of normal children showed that most of the work had been done either on infants (less than 6 months old) or on children who had reached their 9th birthday. In the studies where children from 6 months to 9 years of age were included, one or more of the following were present:

1. The number of children at each year level was small (less than 30 and often only two or three).

2. The results were not entered for each year group separately but were combined (i.e., 0 to 5 years, inclusive).

3. The children were followed over months or years as they matured and many serial tracings on single individuals were entered under different age groups. The resulting figures were not a true measure of variations to be expected in a given number of cases at a given age.

Nicolai and Funaro[1] made the first electrocardiographic studies of children in 1908. Only the standard Lead I was taken on 45 infants. Hecht[2] made a study of 72 children of different ages, but not all of these children were normal. Krumbhaar and Jenks[3] studied 42 normal children and Seham[4] studied 103 normal children. Only 15 of Krumbhaar's and Jenk's cases and 28 of Seham's were in the age group from 6 months to 9 years.

Lincoln and Nicolson[5] studied a group of 222 normal children from 3 to 12 years of age. Four to seven successive tracings were made in as many years in 63 of these. Shookhoff and Taran[6] published their findings on the ECGs of 259 normal children from 6 to 14 years of age, of whom 88 were under 9 years of age. Perry[7] studied the ECGs of 100 normal children from 5 to 13 years of age. Only 22 of the 100 were from 1 to 9 years of age.

Burnett and Taylor[8] investigated 167 healthy children from 3 weeks to 12 years of age. This was primarily a birth to maturity study and serial tracings were taken at inter-

From the Departments of Pediatrics and Medicine, Stanford University School of Medicine, San Francisco, Calif.

Aided by the Commission on Acute Respiratory Diseases, Army Epidemiological Board, United States Army, and by a grant from the Life Insurance Medical Research Fund.

(Received for publication June 24, 1949.)

vals of three months on these children. The greatest number of ECGs on one child was 17 and the average was 7.6 records per child.

Ashman[9] studied the ECGs of 100 normal children. Of these, 49 were in the age group under consideration here. Seventeen cases were from 0 to 5 years and 32 were from 6 to 9 years old. The number of cases in each year age group and the frequency distribution of various measurements were not given.

The work of Burnett and Taylor[8] and that of Lincoln and Nicolson[5] included many ECGs on normal children but the findings are not strictly comparable to the present study as varying numbers of records per child were included. These were serial studies on normal children rather than studies of the variations found in a number of children of a certain age. An individual's serial ECGs were tabulated in the appropriate age group as his age increased and there was no note of how many ECGs a given case contributed nor in how many age groups these tracings appeared. Therefore, these studies do not give a true frequency distribution of measurements at a given age.

Present Study

Clinical Material: One ECG was taken on each of 683 apparently healthy children from 6 months to 9 years of age. Four of these children later were found to have definitely

TABLE I

6 mo. to 1½ yr.	hereafter referred to as 1 yr. age group
1½ to 2½ yr.	hereafter referred to as 2 yr. age group
2½ to 3½ yr.	hereafter referred to as 3 yr. age group
3½ to 4½ yr.	hereafter referred to as 4 yr. age group
4½ to 5½ yr.	hereafter referred to as 5 yr. age group
5½ to 6½ yr.	hereafter referred to as 6 yr. age group
6½ to 7½ yr.	hereafter referred to as 7 yr. age group
7½ to 9 yr.	hereafter referred to as 8 yr. age group

abnormal hearts and were excluded from the total. The remaining 679 cases were tabulated to the nearest birthday and were the basis of this study. Only these 679 ECGs were used in the analysis. When several tracings were made on an individual for the purpose of further investigation, only the first was included, so that the results would represent a true frequency distribution of measurements for a given number of children at a given year of age.

Each year age group represents a 12 months' interval, as shown in Table I, except in the oldest age group which includes children from 7½ to 9 years of age, an 18 month interval.

These were children who had been followed in the Pediatric Clinic at Stanford University Hospitals Out-Patient Department. The tracings were made while they were waiting to be seen in the Children's Clinic for immunization or for periodic check-ups. No child was included who was known to be ill or who had any history or signs of heart disease. The distribution of these 679 cases by age is shown in Chart 1.

Methods

A Sanborne Cardiette (beam galvanometer) was used and the 3 standard limb leads were recorded on photographic film. Most of the children were supine but, to obtain maximum cooperation, some of those from 6 mo. to 2 yr. of age were allowed to sit on the examining table if they preferred.

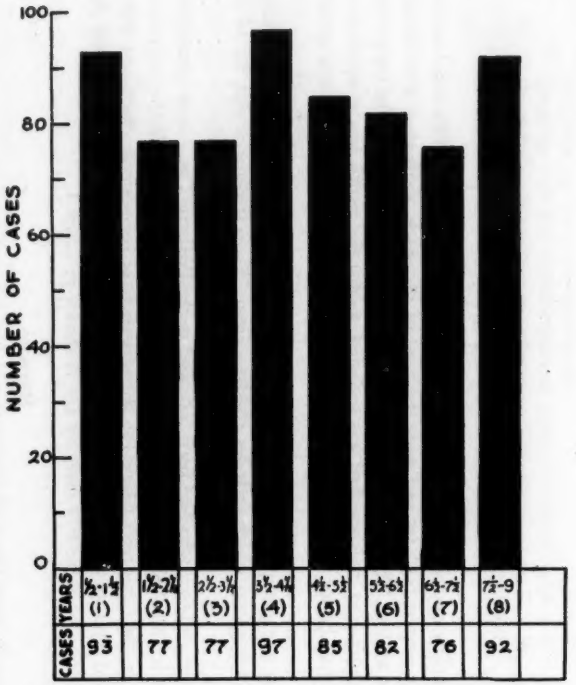


CHART 1. Distribution of Children by Age to Nearest Birthday

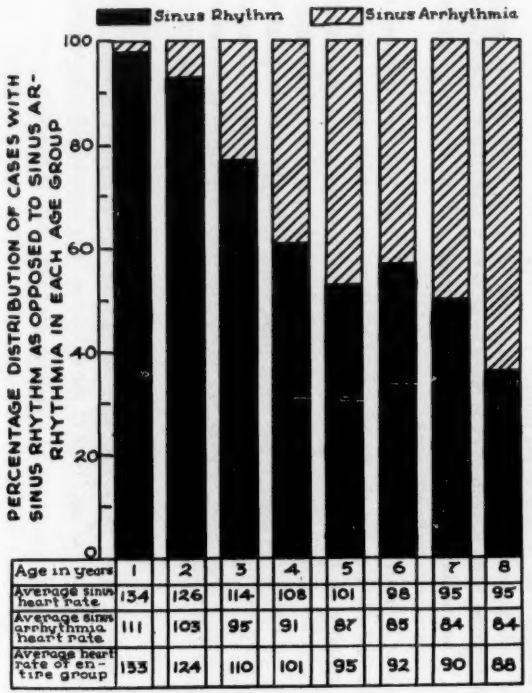

Sinus Rhythm
Sinus Arrhythmia
PERCENTAGE DISTRIBUTION OF CASES WITH SINUS RHYTHM AS OPPOSED TO SINUS ARRHYTHMIA IN EACH AGE GROUP
100
80
60
40
20
0
Age in years 1 2 3 4 5 6 7 8
Average sinus heart rate 134 126 114 108 101 98 95 95
Average sinus arrhythmia heart rate 111 103 95 91 87 85 84 84
Average heart rate of entire group 133 124 110 101 95 92 90 88

CHART 2

TABLE II

AGE, RACE, SEX DISTRIBUTION AND BASIC DATA DERIVED FROM AN ANALYSIS OF ELECTROCARDIOGRAMS OF 679 HEALTHY INFANTS AND CHILDREN

Age in yr.	½–1½		1½–2½		2½–3½		3½–4½		4½–5½		5½–6½		6½–7½		7½–9	
Total Patients:	93		77		77		97		85		82		76		92	
	*	+	*	+	*	+	*	+	*	+	*	+	*	+	*	+
Male	59	63	44	57	39	51	57	59	37	44	46	56	43	57	43	47
Female	34	37	33	43	38	49	40	41	48	56	36	44	33	43	49	53
Negro	52	56	37	48	30	39	41	42	40	47	35	43	35	46	39	42
White	34	37	36	47	42	55	51	53	43	51	45	55	37	49	50	54
Other	7	8	4	5	5	6	5	5	2	2	2	2	4	5	3	3
Sinus	91	98	70	91	59	77	59	61	45	53	47	57	38	50	33	36
Sinus arry.	2	2	7	9	18	23	38	39	40	47	35	43	38	50	59	64
Flat, diphasic or inverted waves																
T3 only	27	29	29	38	27	35	24	25	18	21	15	18	17	23	19	21
P3 only	4	4	3	4	6	8	17	18	16	19	14	17	16	20	15	16
T3 and P3	10	11	9	10	7	9	7	7	8	9	12	15	9	12	3	3
P2 and P3	—	—	—	—	—	—	2	2	—	—	1	1	1	1	2	2
None	52	56	36	47	37	48	47	48	43	51	40	49	33	45	53	58
QRS Interval																
.03 sec.	1	1	—	—	1	1	—	—	—	—	—	—	—	—	—	—
.04 sec.	13	14	5	6	4	5	8	8	9	11	6	7	6	8	5	5
.05 sec.	42	45	28	36	17	22	25	26	20	24	18	22	17	23	14	15
.06 sec.	32	34	37	48	35	45	42	43	35	41	32	39	28	37	38	41
.07 sec.	5	5	7	9	17	22	19	20	14	16	19	23	19	25	24	26
.08 sec.	—	—	—	—	3	4	3	3	7	8	6	7	5	7	11	12
.09 sec.	—	—	—	—	—	—	—	—	—	—	1	1	1	1	—	—
Average QRS	.053 sec.		.056 sec.		.059 sec.		.058 sec.		.059 sec.		.060 sec.		.060 sec.		.062 sec.	
PR Interval																
< .10 sec.	1	1	2	3	1	1	2	2	2	2	—	—	1	1	—	—
.10 sec.	24	26	13	17	11	14	9	9	6	7	6	7	—	—	4	4
.11 sec.	23	25	20	26	13	17	19	20	7	8	13	16	10	13	10	11
.12 sec.	25	27	21	27	20	26	27	28	25	29	19	23	18	24	24	26
.13 sec.	13	14	11	14	17	22	16	16	21	25	22	27	18	24	28	30
.14 sec.	5	5	8	10	12	16	15	15	12	14	15	18	15	20	16	17
.15 sec.	2	2	2	3	3	4	6	6	9	11	4	5	8	11	6	7
.16 sec.	—	—	—	—	—	—	3	3	1	1	3	4	3	4	4	4
.17 sec.	—	—	—	—	—	—	—	—	1	1	—	—	2	3	—	—
.18 sec.	—	—	—	—	—	—	—	—	1	1	—	—	1	1	—	—
Average PR interval	.115 sec.		.117 sec.		.122 sec.		.123 sec.		.128 sec.		.126 sec.		.131 sec.		.128 sec.	

*—Indicates number of cases in a given age group.
+—Indicates percentage in a given age group to nearest whole number.

Regular contact electrodes with electrode jelly were used on the extremities and the ECGs were standardized with 1 mv. equal to 1 cm.

Results

No significant sex or color differences were noted in a preliminary analysis so all the cases were considered together.

Rate and Rhythm: As in earlier studies, sinus arrhythmia was considered present when the difference between the longest and the shortest cycle was 0.1 sec. or more. In general, the cardiac rate decreased as age increased, and with slower cardiac rates sinus arrhythmia was a more frequent finding. In no instance was an abnormal rhythm present. The data are presented in Chart 2.

P Waves: Flat, diphasic or inverted P waves never occurred in Lead I in the 679 ECGs. The P waves were flat, diphasic or inverted in Lead II in 6 cases (2 4-yr. olds, 1 6-yr. old, 1 7-yr. old). There was no reason to suspect heart disease in any of these 6 children. Flat, diphasic or inverted P waves were not uncommon in Lead III. The frequency of these changes in Lead III at each age level is presented in Table II.

T Waves: Inverted, flat or diphasic T waves never occurred in Lead I or in Lead II in the 679 ECGs, but these changes often occurred in Lead III. The incidence of these variations in T_3 are presented in Table II.

ST Segment: The ST segment did not deviate as much as 1 mm. from the baseline in any instance.

Axis Deviation: The axis deviation lay between 0° and 90° in all but 6 of the 679 tracings. Three children showed an axis deviation greater than 90° (98°, 100° and 116°) and 3 children showed an axis deviation less than 0° (−5°, −10° and −30°). These 6 cases are summarized in Table III.

In these 6 cases, the youngest child was 8 mo. of age (1-yr. age group) and could not be located for further study. The other 5 children showing axis deviation were carefully studied and no evidence of heart disease was found. Variations from the usual position of the heart in the chest were demonstrated by the use of unipolar limb and precordial leads in each.[10, 11]

QRS Interval: The QRS interval represents the time required for the electrical impulse to invade the musculature of the ventricles. This measurement is made from the beginning of the QRS complex, whether the first deflection is a Q or an R wave, to its end, whether this is an R, S or S′ wave.[12]

The frequency distribution of QRS values follows a normal curve, the mean increasing with advancing age from .053 sec. to .062 sec. Only 2 were less than .04 sec. (.03 sec. in a 1-yr. old child and in a 3-yr. old), and only 2 were greater than .08 sec. (.09 sec. in a 6-yr. old and in a 7-yr. old). The specific data are presented in Table II and Chart 3.

PR (PQ) Interval: The PR interval represents the time required for the electrical impulse to

TABLE III

Clinical Findings in 6 Cases with Axis Deviation on Standard Limb Leads of Less than 0° or Greater than 90° with Electrocardiographic Position of Heart as Indicated by Unipolar Precordial and Limb Leads

No.	Sex	Color	Age	Ht. (cm.)	Wt. (kg.)	Physical Examination	Electrocardiogram	
							Axis deviation standard leads	Unipolar limb leads and precordial leads to determine electrocardiographic position of heart showed:
1	F	White	1	68	7.7	None	+100°	Unable to locate patient for further study
2	F	Negro	2	83	10.9	Normal	− 30°	Horizontal heart
3	F	White	4	99	16.8	Normal	+ 98°	Semivertical heart
4	F	Negro	4	104	17.7	Normal	− 5°	Horizontal heart
5	F	White	5	117	19.5	Normal	+116°	Vertical heart
6	F	White	5	99	17.2	Normal	− 10°	Semihorizontal heart

travel over the auricle from the SA node to the ventricular muscle. This measurement is made from the beginning of the P wave to the beginning of the QRS complex, whether the first deflection is a Q or an R wave. If there is a Q wave present the measurement is made to the beginning of the Q wave and is sometimes referred to as the PQ interval.[22]

The mere presence of Q waves in a single ECG on a child has little or no diagnostic significance in itself as Q waves are not unusual in ECGs of normal children. When reading ECGs, it is of the utmost importance not to include a Q wave as a part of the PR (PQ) interval, or the resulting (incorrect) measurement may fall outside the expected normal limits.

From 2 yr. through 8 yr. the distribution of PR values follows a normal curve. The curve is skewed to the left in the 1 and 2 yr. groups because the conduction time rarely is less than 0.10

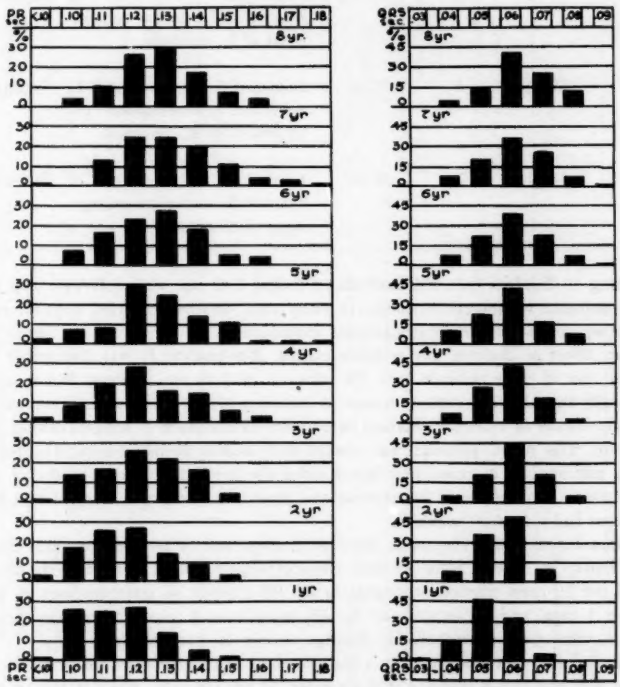


CHART 3. Percentage Distribution of PR and QRS Intervals to Each Year of Age

sec. even in a small heart with a rapid rate. The peak value increases with advancing age through 8 yr. from 0.11 sec. to 0.13 sec. The frequency of occurrence of conduction times shorter than 0.12 sec. becomes less, and that of those greater than 0.14 sec. increases. A value of 0.16 sec. or more is rare in normal children under the age of 9 yr. and is extremely so in children under 4 yr. of age. The data are presented in Table II and Chart 3.

Twenty-three ECGs of the 683 original cases showed PR (PQ) intervals greater than 0.15 sec. Four were found to have definite cardiac abnormalities. Three of these children had probable septal defects and one had sickle cell anemia with an enlarged heart. These 4 children were excluded from the study leaving the total of 679 cases. These 4 cases are summarized in Table IV.

A few children with PR intervals of 0.15 sec. or less may have had some cardiac abnormality which was not discovered on the initial history and physical examination and which did not evidence itself in the ECG. Inclusion of a few of these with the other ECGs did not change the final distribution of measurements to any extent.

TABLE IV

RESULTS OF CLINICAL STUDY OF 4 CHILDREN WITH PR INTERVALS GREATER THAN .15 SEC. WHO WERE FOUND TO HAVE CARDIAC ABNORMALITIES AND WERE EXCLUDED FROM STUDY

Case No.	Sex	Color	Age (yr.)	PR Interval	Roentgenogram and Fluoroscopy	Diagnosis
1	M	White	1	.16 sec.	Generally enlarged heart. Enlarged L. and R. ventricle.	Septal defect
2	F	Negro	3	.16 sec.	Borderline enlargement of heart with borderline enlargement of L. ventricle.	Septal defect
3	M	White	4	.16 sec.	Enlarged heart. Enlarged L. ventricle. Questionable enlargement of R. ventricle.	Septal defect
4	M	Negro	7	.20 sec.	Borderline enlargement of heart with borderline enlargement of L. ventricle.	Sickle cell anemia

The remaining 19 children with PR intervals exceeding 0.15 sec. were followed from 8 to 16 mo. and carefully examined on several occasions. In every case, detailed histories, physical examinations, clinical laboratory procedures, roentgenographic examinations of the chest and serial ECGs were employed in an effort to discover any possible cardiac abnormality. It was impossible to diagnose heart disease in any of these children with PR intervals of 0.16 sec. or more, but it is incorrect to state unequivocally that all were without disease. A summary of these 19 cases is presented in Table V.

There was no history or evidence obtained by physical examination to suggest cardiac decompensation in any case. The blood pressure was always well within normal limits. Thirteen of the 19 children had a soft systolic murmur, best heard along the lower left sternal border or at the apex. Most of these murmurs disappeared on exercise and there was nothing to suggest that any murmur was organic. None had a diastolic murmur.

Possible symptoms of active rheumatic fever in 7 cases, and of possible previous infection with beta Str. hemolyticus in 7 cases, were revealed when extremely careful histories were obtained.

Fourteen of the 19 cases showed no change in the PR interval on serial tracings. A decrease was demonstrated in 1 case, and an increase of the PR interval in 4 cases. Other than the rather long conduction time, there were no remarkable findings on any of these ECGs.

Determination of the ESR was done by a micromethod (Landau-Adams micro-sedimentation rate apparatus) and was considered elevated if it exceeded 10 mm. in 1 hr. Nine of the 19 children had an elevated ESR on one or more occasions. The antistreptolysin titers obtained in 8 cases gave evidence of recent infection with beta Str. hemolyticus (ASL titer greater than 333 u./cc. or a significant increase or decrease on serial examination).[19] Sickle cells were not discovered in the blood of the 10 Negro children by repeated appropriate studies.

Roentgenographic examination revealed no evidence of cardiac abnormality in 10 of these 19 children. In 3 cases there was definite enlargement of the cardiac shadow in some respect. In 6 additional cases there was undue prominence of the pulmonary artery, pulmonary conus or ascending aorta, or borderline enlargement of the cardiac silhouette.

Seven of the children under the age of 4 yr. had PR (PQ) intervals of 0.15 sec. and none had a longer interval (see Table II). If it had been apparent at the time this material was collected that a conduction time of this duration would be rare in this younger age group, these 7 children would have been intensively studied. It was not feasible to have these 7 children return to the clinic when the importance of additional investigation was realized.

QT Interval: The QT interval was recorded for each case. This material is being analyzed and is to be presented at a later date.

TABLE V

RESULTS OF CLINICAL, LABORATORY AND ROENTGENOGRAPHIC STUDY OF 19 CHILDREN WITH PR INTERVALS OF .16 SEC. OR MORE

No.	Sex	Color	Age	Ht. (cm.)	Wt. (kg.)	Syst. murmur	Possible symptoms of active rheumatic fever	Possible previous beta Str. hemolyticus infection	Electrocardiogram		ESR mm./hr.	ASL titer u./cc.	Chest films and fluoroscopy	Additional information of possible significance	Clinical impression+
									First ECG	Later ECG's					
1	F	W	4	109	19.1	+	Transient leg aches	Sore throat with fever	.16	.16	4 13 3	12 12	Normal	Unexplained low fever several times in year studied	A
2	F	W	4	109	19.5	+		Otitis media; impetigo	.16	.16	6 10 5	<12* 166	Normal		B
3	F	N	4	114	23.6	+			.16	.16	8	166* 100	Normal		B
4	F	N	5	119	19.5	+			.16	.16	15 10 6	12 12	Normal		O
5	F	N	5	101	19.5	−	Occas. epistaxis		.16	.16	10 9	166 125	Enlarged heart with enlarged L. ventricle		C
6	M	N	5	111	21.8	+	Occas. leg aches	Frequent sore throat with fever	.18	.20	16 25 21	1250* 1250	Borderline enlargement of L. ventricle. Prominent ascending aorta	Mild anemia for time during study	D
7	M	N	6	106	16.8	+			.16	.18	7 5 5	100 50 100	Borderline enlargement of heart and L. ventricle		B
8	M	N	6	111	19.1	+	Abdominal pain, occas. epistaxis. Occas. leg aches		.16	.16	13 11 13	100 50 100	Normal	Diphtheria aged 3 yr.; severe	B

*—ASL titers indicating recent infection by hemolytic streptococci.

+—Clinical impression is recorded for each case in the following way:

A—Slight suspicion of some active infection, possibly rheumatic fever.

B—Moderate suspicion of some active infection, possibly rheumatic fever.

C—Definite suspicion of some active infection, possibly rheumatic fever.

D—Considered probably rheumatic fever.

O—Considered probably normal.

TABLE V—*(continued)*

No.	Sex	Color	Age	Ht. (cm.)	Wt. (kg.)	Syst. murmur	Possible symptoms of active rheumatic fever	Possible previous beta Str. hemolyticus infection	Electrocardiogram		ESR mm./hr.	ASL u./cc.	Chest films and fluoroscopy	Additional information of possible significance	Clinical impression+
									First ECG	Later ECG's					
9	M	W	6	106	16.8	+			.16	.16	10 4 2	12 12 12	Normal		O
10	M	N	7	126	21.8	—	Occas. epistaxis		.16	.16	13 22 7	333* 333 333	Normal		C
11	F	N	7	126	25.4	—	Occas. epistaxis and leg aches		.18	.18	11	333*	Borderline enlargement of L. ventricle	Later hospitalized elsewhere with impetigo, fever, joint pain. Rheumatic fever?	D
12	F	W	7	114	21.3	—		Occas. fever; sore throat, otitis media once	.16	.14	14 10 6	166 166	Enlarged heart, enlarged L. ventricle		C
13	F	W	7	124	22.7	—	Occas. epistaxis; chorea?	Few bouts of otitis media and sore throat	.16	.16	6	125	Borderline L. ventricle, prominent pulmonary artery and conus		B
14	M	W	7	116	20.9	+			.16	.17	15 10 3	50* 100 125	Normal		B
15	F	N	7	119	20.4	+		Occas. sore throat	.17	.18	10 19 9	50* 166 250 250	Borderline enlargement of L. ventricle		C
16	F	W	8	126	23.1	+			.16	.16	2 3	50 50	Prominent pulmonary artery and conus		A
17	F	N	8	129	21.8	—			.16	.16	10	125	Normal		A
18	F	W	8	132	34.0	+		Occas. sore throat with fever	.16	.16	10 17 20	250 250	Normal		B
19	M	W	8	134	32.7	+		Occas. sore throat	.17	.17	6 8	250* 333	Minimal enlargement of R. ventricle and L. auricle		C

Discussion

One ECG was taken on each of 683 apparently healthy children under 9 years of age. Four of these who had a PR interval of 0.16 sec. or more were shown to have cardiac abnormalities and were excluded from the study, leaving a total of 679 cases. These 679 ECGs were analyzed and the frequency of various findings at each year of age is presented.

T and P waves were frequently flat, diphasic or inverted in Lead III. These changes were never observed in Lead I and rarely in Lead II.

The axis deviation on the standard limb leads was less than 0° in three cases and greater than 90° in three cases. No cardiac abnormality was demonstrated in these six children. Extreme right axis deviation (+130°) is normal for children up to 6 months of age. The axis moves to the left with increasing age so that the average for 1 to 5 years inclusive is +52°.[14] The child who did not return for study was 8 months old and showed a right axis deviation of +100° on the standard limb leads. It is probable that an axis of +100° in this child was not an indication of cardiac disease. The axis deviation in each of the remaining five cases was probably explained adequately by the electrocardiographic position of the heart as demonstrated by unipolar limb and precordial leads.

The frequency distribution of QRS values followed a normal curve. The interval tended to increase slightly with increasing age from 6 months to 9 years. Intervals less than 0.04 sec. or greater than 0.08 sec. occurred in only four cases.

The frequency distribution of PR (PQ) values followed a normal curve from 2 to 8 years. The curve was skewed to the left in the 1 and 2 year group because the conduction time is rarely less than 0.10 sec. The measurement tended to increase with advancing age from 6 months to 9 years. Conduction times exceeding 0.15 sec. rarely occurred in healthy children under the age of 9 years.

Both the PR interval and the QRS interval tended to be longer with increase in height and weight. It was impossible to divorce these changes from those associated with age, since body size becomes greater as the child grows older.

No case was found with all of the diagnostic criteria of a Wolff-Parkinson-White syndrome.

The 23 children with PR intervals of 0.16 sec. or more were studied extensively. Four were found to have definite cardiac abnormalities and were excluded from the main study. The 19 remaining cases were included in the total as no positive diagnosis of heart disease could be made. Some of these may have been abnormal and they are presented in some detail for evaluation and the final clinical impression is recorded.

It is of interest that of 23 apparently healthy children studied because of one finding (a conduction time exceeding 0.15 sec.), only two were perfectly normal as far as could be ascertained and only three had minimal evidence of an active infectious process of an unknown type. In seven there was good evidence, and in five there was definite evidence, of an active infectious process, possibly rheumatic fever. Probable rheumatic fever was the clinical impression in two cases and cardiac abnormality was diagnosed in four children.

Only the four cases with a definite diagnosis of cardiac abnormality were excluded from the frequency tables. Since some of the remaining 19 cases with conduction times greater than 0.15 sec. may not have been healthy, it is apparent that the occurrence of a PR interval of 0.16 sec. or more is rare in a perfectly well child.

Conclusions

An ECG was taken on each of 683 apparently healthy children. Flat, inverted or diphasic T or P waves never occurred in Lead I, rarely occurred in Lead II and frequently occurred in Lead III.

The QRS interval tends to be shorter in children than in adults and increases with age from 6 months to 9 years. Measurements less than 0.04 sec. or greater than 0.08 sec. are rare in healthy children under the age of 9 years.

The PR (PQ) interval tends to be shorter in children than in adults and increases with age from 6 months to 9 years. PR (PQ) intervals of 0.15 sec. or more are rare in healthy children under the age of 4 years. PR (PQ) intervals of 0.16 sec. or more are very rare in healthy children from 4 to 9 years of age.

Acknowledgment

The assistance of Harold K. Faber, M.D., Henry S. Kaplan, M.D., Madoka Shibuya, M.D., Charles E. Duisenberg, M.D., Gordon Williams, M.D., Sally E. Hayes, R.N., and Marjorie Norby, R.N., is acknowledged.

References

1. Nicolai, G., and Funaro, Das Elektrokardiogramm das Sauglings, Zentralbl. f. Physiol. **22**:58, 1908.
2. Hecht, A. F., Der Mechanismus der Herzaktion im Kindesalter, Ergebn. inn. Med. Kinderh. **11**: 324, 1913.
3. Krumbhaar, E. B., and Jenks, H. H., Electrocardiographic studies in normal infants and children, Heart **6**:189, 1917.
4. Seham, M., Electrocardiogram in normal children, Am. J. Dis. Child. **21**:247, 1921.
5. Lincoln, E. M., and Nicolson, G. H. B., Hearts of normal children, Am. J. Dis. Child. **35**: 1001, 1928.
6. Shookhoff, C., and Taran, L. M., Electrocardiographic studies in infectious diseases. I. Normal children, Am. J. Dis. Child. **42**:342, 1931.
7. Perry, C. B., Electrocardiogram of normal school children, Arch. Dis. Childhood. **6**:259, 1931.
8. Burnett, C. T., and Taylor, E. L., Electrocardiograms on 167 average healthy infants and children, Am. Heart J. **11**:185, 1936.
9. Hafkesbring, E. M., Drawe, C. E., and Ashman, R., Children's electrocardiograms: Measurements for 100 normal children, Am. J. Dis. Child. **53**:1457, 1937.
10. Wilson, F. N., and others, Precordial electrocardiogram, Am. Heart J. **27**:19, 1944.
11. Sokolow, M., Present concepts of clinical significance of unipolar precordial electrocardiograms, California Med. **65**:151, 1946.
12. Ashman, R., Essentials of electrocardiography, New York, The Macmillan Company, 1941.
13. Rantz, L. A., Randall, E., and Rantz, H. H., Antistreptolysin "O": Study of this antibody in health and in hemolytic streptococcus respiratory disease in man, Am. J. Med. **5**:3, 1948.
14. Burch, G., and Winsor, T., Primer of electrocardiography, Philadelphia, Lea & Febiger, 1945.

Spanish Abstract

Electrocardiograma en 679 Infantes y Niños Sanos

Se tomó un electrocardiograma de cada uno de 683 niños menores de 9 años de edad aparentemente sanos. Cuatro de éstos que tuvieron un intervalo PR de 0.16 seg. más demostraron tener anormalidades cardíacas y fueron excluídos del estudio, dejando un total de 679 casos. Estos 679 ECG fueron analizados y se presenta la frecuencia de varios descubrimientos en cada año de edad.

Las ondas T y P fueron frecuentemente planas, difásicas o invertidas en Símbolo III. Estos cambios no fueron observados en Símbolo I y rara vez en el II.

La desviación del eje en los símbolos de miembros regulares fué menos de 0° en 3 casos y mayor de 90° en 3 casos. No se demonstró ninguna anormalidad cardíaca en estos 6 niños. Extrema

desviación del eje (+130°) es normal para niños hasta 6 meses de edad. El eje se mueve hacia la izquierda a medida que aumenta la edad así es que el promedio de 1 a 5 inclusive es +52° (14). El niño que no regresó para el estudio tenía 8 meses de edad y mostró una desviación del eje derecho de +100° en los símbolos de miembro regulares. Es probable que una desviación del eje de +100° en este niño no fué una indicación de enfermedad cardíaca. La desviación del eje en cada uno de los 5 casos restantes fué probablemente bien explicada por la posición electrocardiográfica del corazón como se demonstró por los símbolos de miembro unipolar y pr cordial.

La distribución de frecuencia valores QRS siguió una curva normal. El intervalo tuve tendencia a aumentar ligeramente con el aumento de edad de 6 meses a 9 años. Los intervalos menos de 0.04 seg. o mayores de 0.08 seg. ocurrieron solamente en 4 casos.

La distribución de frecuencia de valores PR (PQ) siguió una curva normal de 2 a 8 años. La curva se sesgó hacia la izquierda en los de 1 y 2 años a causa del tiempo de trasmisión que rara vez es menos de 0.10 segundos. La medida tendió a aumentar con el aumento de edad de 6 meses a 9 años. Los tiempos de trasmisión excedieron 0.15 segundos lo que ocurre rara vez en niños sanos de menos de 9 años de edad.

El intervalo PR y el intervalo QRS tendieron a prolongarse con el aumento de altura y peso. Fué imposible divorciar estos cambios de aquellos asociados con la edad, ya que el tamaño del cuerpo se hace más grande a medida que el niño crece.

No se encontró un caso con todos los criterios diagnósticos de un síndroma de Wolff-Parkinson-White.

Se estudiaron extensamente los 23 niños con intervalos. PR de 0.16 segundo o más. Se encontró que cuatro tenían anormalidades cardíacas marcadas y fueron excluídos del estudio principal. Los otros 19 casos fueron incluídos en el total pues no se pudo hacer un diagnóstico positivo. Pueda ser que algunos de éstos hayan sido anormales y se presentan con ciertos detalles para avaluación y se ha puesto en record la impresión clínica final.

Es interesante notar que de 23 niños aparentemente sanos estudiados a causa de nuestro descubrimiento (un tiempo de trasmisión de más de 0.15 segundos), solamente 2 estaban perfectamente normales, según pudimos ascertar, y solamente 3 tuvieron prueba mínima de un proceso infeccioso activo de un tipo desconocido. Hubo buena prueba en 7, y prueba definitiva en 5, de un proceso infeccioso activo, posiblemente fiebre reumática. Posible fiebre reumática fué la impresión clínica en 2 casos y anormalidad cardíaca fué el diagnóstico en 4 niños.

Solamente los 4 casos con un diagnóstico definitivo de anormalidad cardíaca fueron excluídos de las tablas de frecuencia. Como pueda ser que algunos de los 19 casos que quedaron con tiempo de trasmisión mayor de 0.15 segundos no estaban sanos, es aparente que la ocurrencia del intervalo PR de 0.16 segundos o más es raro en un niño perfectamente sano.

2398 Sacramento Street

PAPULAR URTICARIA

Study of the Role of Insects in its Etiology and the Use of DDT in its Treatment

By HARVEY BLANK, M.D., BERTRAM SHAFFER, M.D., MALCOLM C. SPENCER, M.D., AND WILLIAM C. MARSH, M.D.
Philadelphia

PAPULAR urticaria (lichen urticatus) has been a common and puzzling disease of infancy and childhood. Several important characteristics suggest the role of insects in its etiology. It appears during the warmer months, is more common in lower social and economic groups, and usually disappears upon admission to the hospital. In a preliminary report,[1] the authors indicated the importance of flea and bedbug bites in its etiology in confirmation of Dietrich's work,[2,3] and reported their success in therapy with DDT (dichlorophenyl-trichlor-ethane). The present paper is a summary of observations over a three year period.

A child with papular urticaria presents a fairly typical clinical picture. Pruritic skin lesions first appear usually during spring or summer (Chart 1) and crops of new lesions continue to occur in spite of palliative therapy. A history of similar lesions the preceding year is frequently obtained. Persistent discrete questioning of the parents commonly reveals exposure of the child to the common dog or cat flea (Ctenocephalides canis and Ct. felis) or less often to the bedbug (Cimex lectularius) or the human flea (Pulex irritans). This may occur through contact with dogs or cats, sand boxes, coal piles, cellar debris, and such articles as infested upholstered furniture, bedding or heavy pile rugs.

The lesions are characteristically distributed mostly on the arms and legs, particularly on the extensor or exposed surfaces, on the face and neck, and usually least on the trunk (Chart 2). The genital, perianal and axillary regions are almost invariably clear. New lesions are often seen as small (3 to 10 mm.) wheal-like papules which later are rubbed and excoriated. As a result of scratching, many small individual bloody crusts are noted which surmount flattened firm persistent papules or lichens. Secondary infection commonly results in impetiginization and pyogenic ecthymatous ulcers.

Several other skin diseases are frequently confused with papular urticaria. Scabies may mimic it most closely and is differentiated on clinical grounds by the frequent predilection of scabies for the genital, perianal and axillary regions and its rare appearance on the face in children over 3 months of age (Chart 2). In addition, papular urticaria rarely appears in more than one member of a family, in distinction to scabies. If the

---

From the Department of Dermatology and Syphilology, University of Pennsylvania, Philadelphia, Pa.

The following hospitals cooperated in this study: The Children's Hospital of Philadelphia, Hospital of the University of Pennsylvania, Mt. Sinai Hospital, Graduate Hospital of the University of Pennsylvania, and the Skin and Cancer Hospital of Philadelphia.

Presented at the Annual Meeting of the Society for Pediatric Research, Atlantic City, N.J., May 3, 1949.

(Received for publication May 31, 1949.)

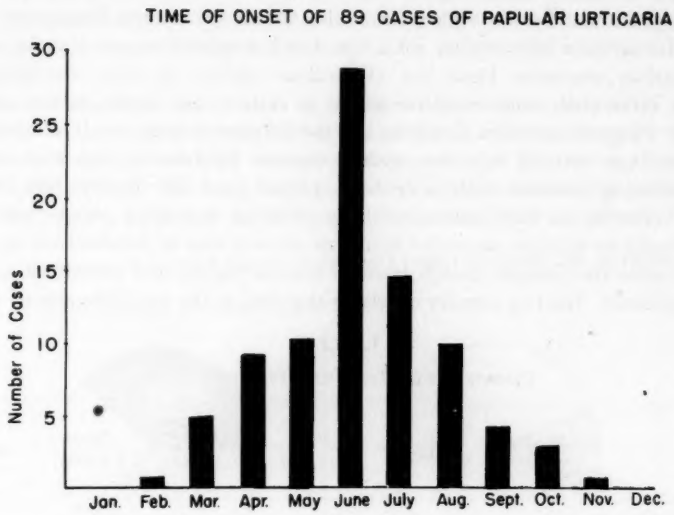


CHART I

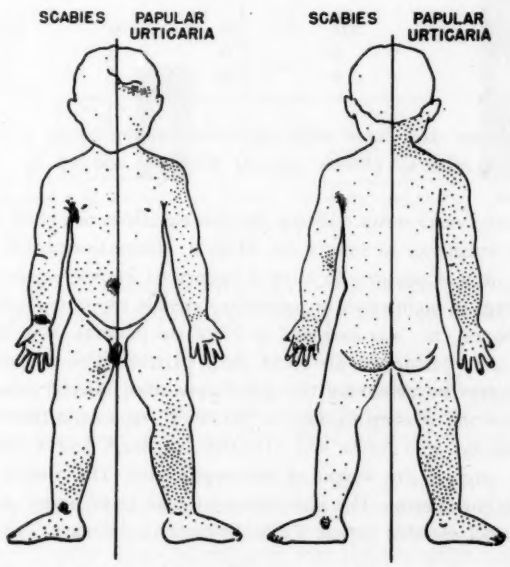


CHART II

diagnosis is in doubt a therapeutic test with a modern scabeticide such as benzyl benzoate is a wise procedure. Because such a lotion also affords a protective film against insects, the papular urticaria may improve for a few days but quickly reappears at the cessation of the scabies treatment. Head lice (Pediculosis capitis) or body lice (Pediculosis corporis) occasionally cause extensive lesions in children and their presence should be ruled out. Pyogenic infections also enter into the differential diagnosis. If adequate measures to eradicate bacterial infections, such as vigorous debridement with soap and water and a softening ointment with or without systemic penicillin therapy, fails to cure a pyogenic infection in the characteristic body areas, an underlying papular urticaria or scabies should be strongly considered. Common urticaria may be differentiated by the fact that its lesions are transient, usually leave no residual papules and are seldom excoriated or impetiginized. The tiny papules or wheals that may be the manifestations of ordinary

TABLE I

RESULTS OF SKIN TESTS WITH INSECT ANTIGENS

	Diluent	Flea 1:5,000	Flea 1:10,000	Cimex 1:5,000	Flea and/or Cimex
Patients with papular urticaria					
No. patients tested	30	12	17	30	30
No. patients positive	0	10	9	10	23
% patients positive	0	83	53	33	77
Control subjects					
No. subjects tested	124	28	96	124	124
No. subjects positive	0	0	0	2	2
% subjects positive	0	0	0	2	2

urticaria in infants are distributed most commonly on the trunk, in distinction to the "centrifugal" distribution of chronic papular urticaria, and do not result in chronic lichenified papules.

Although the exact mechanism whereby this disease affects one child in a family is not certain, abnormal sensitivity to insects can often be demonstrated. Of 87 patients with papular urticaria, it was possible to elicit a history of known exposure to fleas in 26 cases and to bedbugs in eight cases. In addition, possible exposure, from the presence of cats, dogs, sand boxes, etc., was indicated in 72 of the patients. Skin tests with flea and bedbug antigens were performed on 30 of these patients. The antigens were prepared according to Cherney[4] by extracting the dried pulverized insects with phenol 0.5% in saline for 48 hours and passing through a "Swinney" type Seitz filter. The extract was prepared in a dilution of 1:5,000 and 1:10,000 for flea,* and 1:5,000 for bedbug,† calculated on the original dry weight of the insects used. The control solution was the phenol 0.5% in saline diluent. The skin tests were read in 48 hours. A positive reaction consisted of a distinct elevated papule 3 mm. or more in diameter. Table I indicates that

* The flea antigen was prepared from cat fleas (Ctenocephalides felis) supplied by W. V. King, U. S. Dept. of Agriculture, Agricultural Research Administration, Bureau of Entomology and Plant Quarantine, Orlando, Fla.

† The bedbug (Cimex lectularius) antigen was prepared from material supplied by Frank O. Hazard, Wilmington College, Wilmington, Ohio.

77% of the patients with papular urticaria were sensitive either to flea or cimex or to both. In a control series of 124 subjects, most of whom were children in corresponding age groups, only two had positive skin tests. These studies will be reported in greater detail elsewhere.

To insure unequivocal results from an evaluation of treatment with DDT, no other medications of any type were used during the period of observation, and each patient was followed carefully at weekly intervals. The parents were given an instruction sheet with a supply of DDT 5% in talc to be used as a dusting powder on the patient and in his bedding. At the beginning of the study, a few patients were treated with DDT 5%

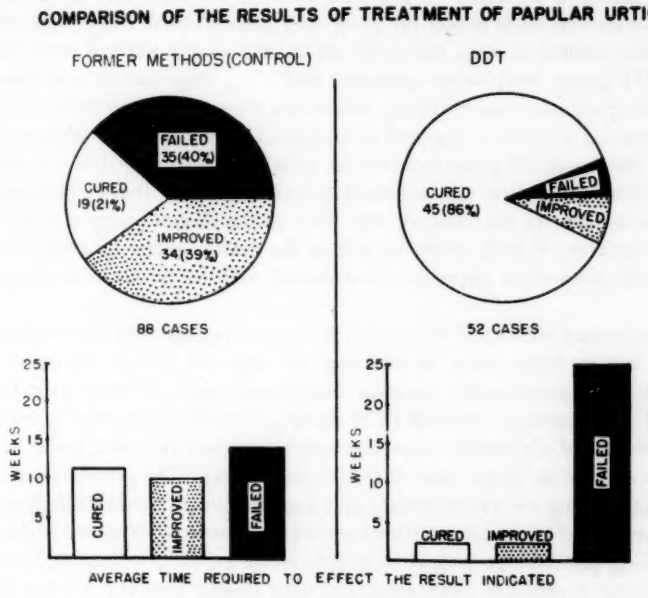


CHART III

in a shake lotion, but this was discarded to obviate the remote possibility that the lotion itself might have some beneficial effect. The instruction sheet read as follows:

PAPULAR URTICARIA

This is a disease of the skin. It is usually caused by sensitivity to insects. The common insects that cause it are fleas from dogs, cats, house, sand or other humans; as well as bedbugs and possibly other insects. It is necessary, therefore, for you to remove all sources of these insects.

INSTRUCTIONS

1. A *spray* of 5% DDT in Flit is to be used daily in your household. The baseboards, the cellar, the bed frames and upholstered furniture should receive special attention.
2. A *powder* of 5% DDT should be dusted on dogs and cats, under cushions and rugs, and wherever the spray cannot be used.
3. Contact with dogs and cats should be avoided.
4. All collections of sand should be removed.
5. The child should be dusted lightly with the special powder which will be prescribed. This powder should also be dusted on his bed clothes and mattress.

Note: Be certain to check the label of the sprays and powders you buy. Be sure that they contain DDT and in at least 5% strength.

Precautions

1. When spraying with DDT, make certain that food, dishes and cooking utensils are protected from the spray. Avoid direct contact with the spray and ventilate the room after the spraying.
2. To avoid eating of the DDT powder by cats: after dusting the fur, the excess powder should be removed with a damp cloth.
3. The powder should be dusted very lightly on the child as only the barest film is necessary.

The results of 54 patients treated with the DDT regime and 88 by a variety of other methods are indicated in Chart 3. All patients were included for whom adequate follow-up examinations made it possible to record a definite result. There were approximately an equal number of boys and girls; about 60% of the patients were Negroes.

Of the DDT group, 86% were considered cured, i.e., they had no new lesion and experienced complete cessation of itching within two weeks. Although 21% of the controls were appraised as cured, it required an average of 11 weeks before this result could be recorded. The improved group included the patients in whom there was a reduction in pruritus but in whom there was continued appearance of new lesions, although these were fewer in number. In this category were 39% of the control group and 8% of the DDT treated patients. A study of the records of the control group indicated that many of these patients got well or improved spontaneously with the termination of the insect season.

The patients treated with DDT who failed to respond rapidly were followed carefully in the clinic and by home visits. In this way, one apparent failure was cured by the purchase of a new mattress when, for some unexplained reason, bedbugs were found in the depths of the mattress in spite of DDT dusting. The three persistent failures were seen for an average of six months. These apparently represent the small group in whom the disease is induced by agents other than the above insects. The persistence of lesions in these patients during the winter months also suggests this. In the DDT failure group, two patients responded by partial and temporary improvement to an elimination diet, while in the remaining patients new lesions were induced by exposure to heat or by wearing excessive clothing. A complete disappearance of these lesions, however, was not obtained by reducing these factors.

Conclusions

Papular urticaria (lichen urticatus) is a chronic disease which in the great majority of cases occurs during the warm seasons on exposure to fleas and bedbugs.

Skin tests indicate many such patients are abnormally sensitive to these insects.

In the three year study reported, it was demonstrated that 86% of the patients could be cured in two weeks with a 5% DDT dusting powder and DDT household spray, whereas with former methods of therapy, only 21% were cured in 11 weeks of treatment.

References

1. Shaffer, B., Spencer, M. C., and Blank, H., Papular urticaria: Its response to treatment with DDT and role of insect bites in its etiology, J. Invest. Dermat. **11**:293, 1948.
2. Dietrich, A., Hautreaktionen nach Ungezieferbissen, Monatschr. f. Kinderh. **75**:70, 1938.
3. Dietrich, A., Hautreaktionen nach Ungezietersticken unter dem Bildeiner Lichen Urticatus, Arch. f. Dermat. u. Syph. **182**:668, 1942.
4. McIvor, B. C., and Cherney, L. S., Studies in insect bite desensitization, Am. J. Trop. Med. **21**: 493, 1941.

SPANISH ABSTRACT

Urticaria Papular: Un Estudio del Papel que Insectos tienen en Su Etiología y el Uso de DDT en Su Tratamiento

La urticaria Papular (*Lichen urticatus*) es una enfermedad crónica en la mayor parte de casos ocurre durante las estaciones calientes al exponerse a moscas y chinches.

Ensayos de la piel indican que muchos de estos pacientes son anormalmente sensibles a estos insectos.

En un estudio de 3 años se ha demostrado que 86% de los pacientes pueden ser curados en 2 semanas con un 5% de polvo DDT y rociados de casa DDT, mientras que con los métodos antiguos de terapia, solamente un 21% fueron curados en 11 semanas de tratamiento.

University of Pennsylvania

CARDIO-ESOPHAGEAL RELAXATION (CHALASIA) AS A CAUSE OF VOMITING IN INFANTS

By WILLIAM BERENBERG, M.D., AND EDWARD B. D. NEUHAUSER, M.D.
Boston

THE problem of persistent or recurrent vomiting in the newborn or young infant is encountered frequently in pediatric practice. It may be produced by a variety of causes. It is due often to parenteral factors and the majority of these infants are never studied by roentgen methods. The vomiting in many instances is never severe or frequent enough to merit roentgenographic examination. However, there are infants who continue to vomit repeatedly without any satisfactory explanation. Roentgenologic study is warranted in this latter group. During the past five years we have observed 24 patients in this group with repeated vomiting apparently due to persistent relaxation of the hiatal portion of the esophagus with failure of the gastric cardia to perform its usual "sphincter" action. We have previously described a smaller series[1] of patients exhibiting this syndrome in whom the persistent relaxation was termed "chalasia" since in many respects it appears to be the opposite of achalasia or cardiospasm.

The etiology of this syndrome is uncertain and one can only speculate on the basis of the various theories of closure of the cardia. Several of these theories have been reviewed elsewhere.[1, 2] The normal hiatus esophagus does not gape, but, as Jackson[3, 4] states, is closed by a pinchcock-like action of the diaphragm. This action depends on special diaphragmatic muscle bundles surrounding the lower esophagus and acting to open and close the cardias.[5] The type of persistent relaxation of the sphincter action under discussion could of course be produced by improper muscular development or imbalance of neuromuscular control.

In normal deglutition this muscular sphincter relaxes to allow the passage of food into the stomach. If it fails to close, gastric contents will reflux into the esophagus, resulting in regurgitation. This may well be aggravated by the differences in pressure in the thoracic and abdominal portions of the esophagus.[6] On inspiration there is a reduction of intrathoracic pressure and an increase in intra-abdominal pressure. This should favor free reflux of gastric contents into the esophagus. Actually this does occur in chalasia, but not in the normal child due to the efficiency of the pinchcock-action of the sphincter. It should be emphasized that there is no anatomically demonstrable circular muscle band at the cardia[7] and that what is referred to as a sphincter is really the action of the muscle bundles of the diaphragm resulting in changes in the size of the hiatus esophagus.

The neuromuscular control of the cardia is such that vagal stimulation or sympathetic inhibition will produce relaxation of the cardia while vagal inhibition or sympathetic stimulation leads to contraction.[8] This has been confirmed[9] by excision of the sympathetic fibers surrounding the celiac axis and left gastric arteries in cats. Such an operation re-

From the Departments of Pediatrics and Radiology, Harvard Medical School, and The Children's and Infant's Hospitals, Children's Medical Center, Boston, Mass.

Read at the 59th Annual Meeting of the American Pediatric Society, Atlantic City, N.J., May 6, 1949.

(Received for publication June 30, 1949.)

sulted in a patulous relaxed cardia affording easy gastric regurgitation. The tone of the cardia may also be relaxed by mild stimulation of the gastric mucosa and by oral and pharyngeal sensory impulses. These again probably act through sympathetic-parasympathetic channels.

Two patients in this series had obvious intracranial damage with mental retardation. In both instances the repeated vomiting and persistent relaxation observed on barium swallow lasted for several months beyond the expected termination of the syndrome. It is interesting to speculate that in these patients there was central interference with the normal nervous control of the pinchcock action.

One patient in this series had repeated severe vomiting until 8 months of age with relaxation of the cardia demonstrable on repeated examinations. Finally a small filling defect of the distal esophagus was found on barium swallow which was identified on esophagoscopy as a hemangioma. After removal of this lesion the vomiting ceased and subsequent roentgenographic study showed normal tone of the cardia. This raises the possibility of local esophageal abnormalities resulting in persistent relaxation of the cardia due either to local irritation or to interference with normal myenteric plexus control.

The clinical findings and course of the 24 infants reviewed in this series forms a well defined syndrome. The prenatal course was normal in all instances as far as known. Careful inquiry as to the birth itself revealed an unusually difficult delivery necessitating prolonged resuscitation of the infant in only three instances. The condition was seen with equal frequency in male and female infants. In most instances the feeding regime during the first few days was not unusual. Almost all the infants had not received anything by mouth for 12 to 24 hours and were then offered glucose or lactose in water for a 12 to 24 hour period before milk formulas or breast milk feedings were instituted.

The patient invariably begins to vomit within 10 days after birth and usually within three days. Vomiting becomes progressively worse and soon occurs with most feedings although occasionally two or three successive feedings may be retained. The infant appears otherwise well, active and hungry. The vomiting seems effortless and rarely is forceful or projectile. The vomitus does not contain bile although gastric secretions may be visible in the material. Although vomiting may take place during a feeding and while the infant is actively sucking, it is more apt to occur when air is expelled or when the baby is put back in his crib in the supine or decubitus position. The entire feeding may be vomited at this time or there may be repeated regurgitation of parts of the ingested meal during the period between feedings. Occasionally the mother may remark that as long as she holds the infant upright food is retained but vomiting starts with recumbency. Physical examination reveals no abnormalities other than occasional instances of malnutrition or dehydration resulting from lack or loss of food.

Extensive studies in all cases were carried out to investigate other possible causes of vomiting. Complete blood and urine studies showed no significant variations from the normal. Serum electrolyte determinations were abnormal only when vomiting had been severe enough to produce the changes ordinarily associated with starvation. Lumbar puncture was done in the vast majority of patients and revealed normal cerebrospinal fluid. Subdural taps were performed on five infants and no fluid was obtained in any instance.

Untreated, the patient either lost weight or gained slowly over a period of many weeks. Various attempts to prevent vomiting by food changes were unsuccessful. In many instances the infant was taken off all oral feedings and maintained with parenteral fluids

only to have the vomiting recur with the return to feedings of small amounts of water or 5% glucose in water. The response to specific management was immediately and strikingly beneficial in all instances.

The most important diagnostic aid is adequate fluoroscopic examination of the swallowing function, esophagus and stomach (Figs. 1 and 2). A sufficient quantity of barium is mixed with the formula or with 5% glucose and the mixture is fed through an ordinary nursing bottle. Heavy mixtures of barium should not be employed. Under fluoroscopy there is diminished intensity and frequency of esophageal peristalsis. The esophagus is larger than usual and gives the impression of being thin-walled and flaccid. There is persistent failure of the "sphincter" or "pinchcock" action to occur. As a result

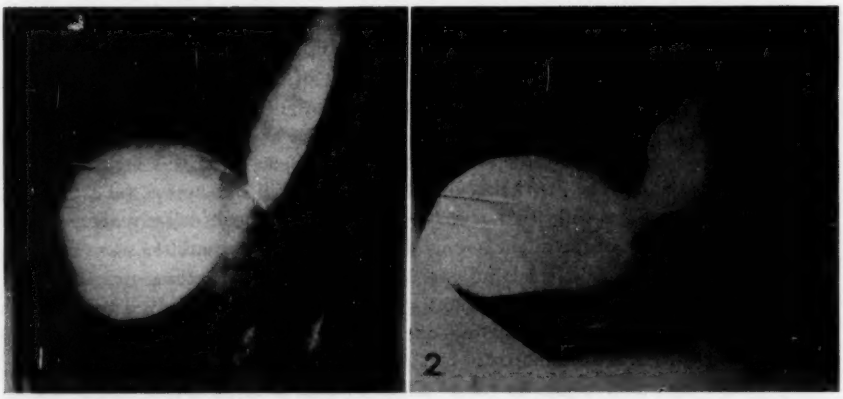


FIG. 1. R. H., aged 12 days. Normal emptying of stomach but with moderate cardio-esophageal relaxation.

FIG. 2. H. P., aged 8 days. Relaxation of hiatus esophagus. Retrograde filling of esophagus occurred during inspiration and also from slight pressure upon abdomen.

of this one visualizes the esophagus as a dilated flaccid tube leading to the gastric cardia. With the inspiratory phase of respiration the esophagus dilates further and barium may be seen to enter it from the stomach since there is no mechanism to prevent regurgitation of gastric contents. During the expiratory phase of respiration the filled esophagus is compressed and some barium is regurgitated up into the mouth while some is forced back into the stomach. With the patient recumbent even slight pressure upon the abdomen produces retrograde filling of the esophagus with gastric air or barium. The same thing occurs when crying or struggling result in increased intra-abdominal pressure. One does not see the changes associated with ordinary vomiting, such as diaphragmatic contraction or reverse peristalsis with gastric contraction unless the regurgitation initiates real gagging followed by true vomiting. No regurgitation is noted if the patient is studied in the erect position although the persistent cardio-esophageal relaxation is evident and one may readily visualize air passing into the esophagus from the stomach.

The roentgenologist must be familiar with the appearance of the normal esophagus in infants.[10] The roentgen appearance must be differentiated from that encountered in other conditions. In patients with congenitally short esophaguses the persistent vomiting is of longer duration and frequently associated with hematemesis. On barium roent-

genographic studies there may be visible gastric striae in the supradiaphragmatic portion of the stomach and the appearance of one or two strictures. Symptoms produced by this condition may manifest themselves first at any age but most commonly do so during late childhood or adult life.

The roentgen appearance of a partial supradiaphragmatic stomach due to diaphragmatic hernia is rarely seen in infancy and can usually be recognized with ease. Rather persistent relaxation of the hiatus esophagus may occur in association with obstruction of the pylorus or duodenum but it is evident that it represents a secondary phenomenon.

FIG. 3. J. P., aged 8 days. Patient kept in sitting position in crib.

The chief complications encountered in this series have been dehydration, failure to gain weight and rarely mild acidosis. In a few instances there have been pulmonary changes due to aspiration pneumonitis. One of the patients, previously referred to as having associated cerebral damage, developed a tendency to rumination. There were no deaths in this series. The only esophagoscopy performed was in the one patient with hematemesis due to hemangioma of the esophagus. Unlike the cases reported by Wyllie and Field,[2] hematemesis was not observed in any of the other patients.

Drugs of the atropine and prostigmine groups were employed without alteration of the clinical course of this syndrome. No change occurred after various milk formula modifications or the substitution of breast milk feedings or 5% glucose in water for the formula. Relief of symptoms has been achieved so far only by empiric measures. The patients are fed in a sitting or semi-erect position and kept in this position for 30 minutes after the feeding has been finished. Feedings are thickened with one ounce of cereal to 15 ounces of formula. This is done to obtain a heavier mixture than the ordinary milk modification with the idea that such a mixture would be less likely to reflux through the relaxed cardia. The infant is then kept propped up in the crib by use of pillows and a harness-like support (Fig. 3). He is usually kept in this position throughout the major

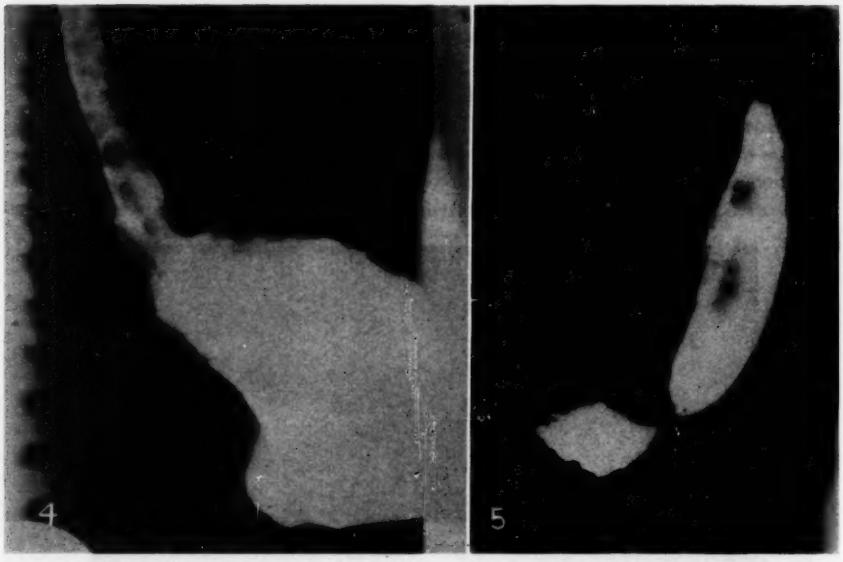


FIG. 4. R. P., aged 6 days. Moderate relaxation of cardia. Reflux filling produced by abdominal pressure.

FIG. 5. R. P., aged 3 mo. Asymptomatic for 6 wk. No cardio-esophageal relaxation or reflux filling.

part of the day and night. Patients with milder variants of this syndrome need only to be maintained in the erect position for a period of 30 to 60 minutes after feedings. Others may be corrected simply by thickening the feedings alone. This regime may be easily carried out at home.

On such an empiric therapeutic regimen all of the infants stopped vomiting immediately and began to gain weight and to develop normally. In most instances therapy could be discontinued after 3 to 4 weeks. Repeat roentgenographic studies carried out after that time usually revealed either striking improvement or a normal appearance (Figs. 4 and 5). Of those patients in whom subsequent barium swallows failed to show improvement in esophageal function, one had an obvious cerebral defect, another had a hemangioma of the esophagus, and the third remains without specific explanation 1½ years after birth, although her vomiting stopped with therapy and has not recurred.

DISCUSSION

The patients presented in this report appear to represent a clinical syndrome by virtue of their common symptomatology, course, roentgenographic findings and response to defined although empiric therapy. The etiology is uncertain and probably multiple. From the nature of the syndrome and its self limited course in most instances it would appear likely that it is most often produced by a temporary neuromuscular dysfunction. In other instances exemplified by patients with esophageal hemangioma and a cerebral defect there is probably a more persistent imbalance produced by the specific organic disturbance. Both

the temporary functional and the persistent organic theories of causation may be correlated with the various theories concerning physiologic control of closure or relaxation of the cardia.

Milder variants of this syndrome are probably more common than is ordinarily recognized. This is borne out by the number of cases of well established chalasia diagnosed once we became aware of its existence. Many pediatricians will recall any number of infants who had to be held erect by the mother for a period of time after feedings because the mother learned that the baby would vomit if he was immediately placed in his crib. The story of infants who regurgitate or vomit part of all milk feedings but retain them when cereal or other solids are added is a familiar one. Again we all have seen children who regurgitate appreciably until they reach the age when they assume the erect position for a major part of their wakeful day. Many of these might be milder variants of the chalasia syndrome.

Summary and Conclusions

Repeated vomiting in the newborn or young infant may be produced by persistent relaxation of the hiatus esophagus. Twenty-four patients with this condition have been observed during the past five years. Milder variants may occur more often than have been recognized.

The syndrome in the majority of patients is produced by a temporary neuro-muscular dysfunction. When some organic defect such as a congenitally short esophagus is the causative factor the condition is more apt to be persistent or to start later in life.

The diagnosis is suggested by persistent, otherwise unexplained vomiting which can be alleviated by keeping the patient in an erect position. An absolute diagnosis can be made only by fluoroscopic examination with a barium swallow. The diagnostic change is persistent relaxation of the hiatus esophagus with retrograde filling of the esophagus during inspiration or with increase in intra-abdominal pressure.

Therapy is empiric and consists of the use of thickened formulae and of keeping the patient in the erect position, particularly after feedings.

References

1. Neuhauser, E. B. D., and Berenberg, W., Cardio-esophageal relaxation as cause of vomiting in infants, Radiology **48**:480, 1947.
2. Wyllie, W. G., and Field, C. E., Etiology of intermittent oesophageal regurgitation and haematemesis in infants, Arch. Dis. Child. **21**:218, 1946.
3. Jackson, C., Diaphragmatic pinchcock in so-called "cardiospasm," Laryngoscope **32**:139, 1922.
4. Jackson, C., and Jackson, C. L., Bronchoscopy, Esophagoscopy and Gastroscopy, Philadelphia, W. B. Saunders Company, 1934.
5. Hurst, A. F., and Stewart, M. J., Gastric and Duodenal Ulcer, New York, Oxford University Press, 1929.
6. Negus, V. E., Mechanism of swallowing, Proc. Roy. Soc. Med. **36**:85, 1942.
7. Lendrum, F. C., Anatomic features of cardiac orifice of stomach, Arch. Int. Med. **59**:474, 1937.
8. Best, C. H., and Taylor, N. B., Physiological Basis of Medical Practice, Baltimore, Williams & Wilkins Company, 1945.
9. Knight, G. C., Relation of extrinsic nerves to functional activity of oesophagus, Brit. J. Surg. **22**:155, 1934.
10. Bakwin, H., Galenson, E., and LeVine, B. E., Roentgenographic appearance of esophagus in normal infants, Am. J. Dis. Child. **68**:243, 1944.

SPANISH ABSTRACT

Relajación Cardio-Esofágica (Chalasia) como una Causa de Vómito en Infantes

Vómitos recurrentes en el infante pequeño puede ser debida a una gran variedad de causas. Durante un período de estudio de cinco años, 24 pacientes han sido observados y seguidos en quienes la disfunción era producida por una relajación de la porción hiatal del esófago con fracaso de la acción "esfínter" normal de la cardia. La condición ha sido determinada "chalasia"—el contrario de achalasia.

Este síndroma es producido por un trastorno automático de ya sea la estimulación vagal o la inhibición simpática. Otras anormalidades anatómicas o fisiológicas de menor importancia pueden también desempeñar un papel etiológico.

El vómito persistente generalmente principia dentro de la primera semana de vida y se vuelve progresivamente peor. Está más apto a ocurrir cuando el aire es expelidos o cuando el paciente está en una posición supina. El exámen físico y otros estudios invariablemente no son revelantes. El examen fluoroscópico de la función de tragar con bario revela trastorno persistente de la acción "pinchcock" de la cardia. Durante la inspiración el esófago se dilate y se llena con bario desde el estómago. Durante la expiración, el esófago lleno se comprime. Con el paciente en la posición supina, el envase retrógrado del esófago puede ser producido por un aumento en la presión intra-abdominal.

Todos los pacientes han respondido bien a un régimen empírico bajo el cual se les alimenta con alimentos espesos y se les mantiene en posición erecta por un período prolongado después de la alimentación. La repetición del examen fluoroscópico algunos meses más tarde generalmente revela que no hay anormalidad.

300 Longwood Avenue

PLACE OF ORAL FEEDING IN INFANTILE DIARRHEA

By ARTHUR W. CHUNG, M.D., AND L. EMMETT HOLT, JR., M.D.
New York City

A LITTLE more than a year ago one of us (A. W. C.) presented evidence[1,2] indicating that the customary practice of treating infantile diarrhea by a period of oral starvation followed by gradual resumption of full oral feeding was not a sound one. It was shown (1) that the intolerant intestine absorbed more food when more was given and (2) that recovery of tolerance was not delayed by oral feeding. Since this publication early oral feeding has received both favorable[3–5] and unfavorable[6,7] comment. For the former we are most appreciative. To our critics it has seemed desirable to reply in order to clarify what appear to be misinterpretations of our data and conclusions.

Freudenberg,[6] lamenting the current nihilistic attitude toward scientific infant feeding, cites as the acme of radicalism the regimen of Chung and Viscorova—feeding 80 cal./kg. immediately after interruption of intravenous therapy. He criticizes their work because mild cases were included with toxic ones, and he regards an over-all mortality of 10% as excessive, particularly since the clinical material consisted predominantly of older, breast-fed infants.

Freudenberg was mistaken in concluding that the infants studied in Bratislava were predominantly breast-fed; practically all were artificially fed. He is correct in pointing to a higher mortality than that reported from many university clinics for reasons not altogether clear. It is definitely higher than our current mortality at Bellevue Hospital using the regimen of Chung and Viscorova. However, the higher mortality in Bratislava can scarcely be attributed to the feeding since an almost identical mortality was observed on both feeding regimes studied; the mild and toxic cases were equally distributed in the two groups.

A second criticism comes from Darrow and his collaborators[7] who, in an admirable and exhaustive study of water and electrolyte metabolism in eight cases of infantile diarrhea, reaffirm the time-honored view that the resumption of oral feeding before intestinal tolerance is regained is dangerous and may precipitate dehydration and acidosis. They find support for this view in their material as well as in the published data of Chung. Since the data in question appear to be susceptible to differences in interpretation, we have attempted to analyze the evidence in further detail.

Among the cases studied by Darrow et al.,[7] the following are cited as illustrating the untoward effects of early feeding:

Case 1, when shifted from a regime of oral starvation and parenteral fluids to one of increasing oral food, showed an increase in stool water and a negative total water balance.

Case 4, a severely dehydrated infant, was given oral starvation and parenteral fluids for 2.54 days, followed by a period of three days of increasing oral food, after which full oral feedings were given. Coincidental with the resumption of full oral feedings

From the Department of Pediatrics, New York University-Bellevue Medical Center, New York, N.Y.

(Received for publication July 11, 1949.)

the volume of the stools increased with loss of considerable K by this route; the patient's appearance deteriorated, there was increased sweating and a fall in the plasma bicarbonate developed. Subsequently after a period of fasting (? with parenteral fluids) recovery occurred.

Case 5 likewise showed an increased loss of water by bowel on passing from a period of increasing oral feeding to one of complete oral food.

Case 7 showed a clinical and chemical relapse when oral food was first started after the period of oral starvation and parenteral therapy. The fecal fluid was notably increased with resumption of oral feeding.

Case 8 developed diarrhea and dehydration while on a full caloric regimen, the only period studied.

In commenting on the data of Chung, Darrow et al. cite as evidence of the danger of oral therapy the resulting increased losses of water and electrolytes in the stool, the failure to achieve electrolyte balance even on high feedings, and low urine volumes in several instances. The presumption is that oral feeding brought these patients closer to dehydration.

In reviewing the evidence referred to above it is clear that untoward effects in the direction of dehydration occurred in some instances and may have been imminent in others. It is also clear that in the studies of Darrow et al.,[7] a number of variables were simultaneously altered, and it appears to us that factors other than the alteration of the food provide an adequate explanation of the dehydration in every instance. For example, one may note in passing that in the two instances in which clinical dehydration developed following an increase of food (Cases 4 and 7), a simultaneous reduction in the total water intake had been made which alone might have been sufficient to precipitate dehydration. In Case 8 the total fluid intake during the critical period was apparently only 267 gm./day! Of the increased negative water balance in Case 1 a negligible part (43 gm.) was due to stool loss, whereas increased sweating accounted for almost four times this figure. The thesis that oral food was responsible for this increased water loss by sweating would seem questionable in view of the absence of meteorologic data and the fact that this phenomenon occurred with no regularity.

A more cogent consideration is the fact that in every one of the cases treated by Darrow et al.,[7] the introduction or increase of oral food was accompanied by a decrease in parenteral fluid. It is obvious that if the substitution of oral for parenteral fluid were made before the intestine had regained its tolerance, increased water loss from the gut would result and dehydration might develop. The premature substitution of oral for parenteral fluid, electrolyte or food may thus be hazardous, we will agree. This is quite a different proposition from attributing dehydration to oral feeding *per se*. We would regard the untoward phenomena observed by Darrow et al.[7] as due primarily to premature withdrawal of parenteral therapy rather than to premature oral therapy. The substitution of oral for parenteral therapy is something we have never recommended and have taken pains to state that we were not recommending. Our thesis had to do with the safety and the value of the oral route as an adjuvant to needed parenteral therapy.

Turning to the metabolic data of Chung, it appears that our critics have failed to grasp the purpose of these studies. They were designed not to demonstrate ideal therapy, but to evaluate one variable—oral feeding—other things remaining constant. As far as we are aware, they are the only studies so designed. To accomplish this purpose obviously desirable parenteral therapy was withheld for brief periods. This made it possible to study

absorption without the complication of excretion of parenterally administered water and electrolytes into the gut. It is true that deficits of Na, K, Cl and H_2O in some cases were not corrected by oral feeding alone, but the fact remains that the balances were improved in every instance by oral feeding. The more voluminous stools, though alarming on the diaper, actually signified better net absorption of foodstuffs.

The existence of a relapse in diarrhea is difficult to establish. A relapse may be defined as a loss of intestinal tolerance. One should not conclude that a relapse exists merely because manifestations of diarrhea increase with an increased oral intake for this does not mean that tolerance is falling, merely that it is being more rigorously tested. Such a situation is only an apparent relapse. The existence of a true relapse can be established only when under fixed conditions of intestinal load there occurs increased stooling. From the evidence presented we are inclined to believe that true relapses did occur in the series of Darrow et al.[7] though it is difficult to be certain about this. But even if one were to grant (which we do not) that all the increases in stool output associated with food were due to real loss of tolerance rather than to apparent relapse, the conclusion that real intolerance was induced by the food is not justified. Against this conclusion may be cited the known unpredictable course of the disease, a variability demonstrated clearly in this small series where the administration of food, increasing at an identical rate, although followed by apparently unfavorable results in some cases was followed by extraordinarily favorable ones in others. Thus in Case 2 (period 2) the administration of food was accompanied by a decrease of stool water from 352 to 39 gm./day! In Case 3 (period 3) the stool water fell after feeding to half the preceding volume and in Case 6 (period 2) it fell either to zero or to an unrecorded value. If the doctrine of *post hoc, ergo propter hoc* is to be applied here, it would seem that it should be applied to all cases regardless of the outcome.

It has been our impression for some time past that true relapse in diarrheal states was due to the vagaries of the disease, being unrelated to the oral food load. The opportunity to verify this impression presented itself in Bratislava in 1947 where it was possible to determine the duration of the disease in a large group of cases treated alternately by full feedings from the start and by the conventional therapeutic starvation regimen. If the oral feedings had induced relapse or delayed recovery of tolerance the duration of the disease in that group should have been greater, which was not found to be the case. If anything, the duration was shorter in the cases receiving full oral feedings throughout.

In conclusion, although disagreeing with Darrow et al.[7] on the question of oral feeding, we should like to express our hearty agreement with these investigators as to the cause of death in fatal cases of diarrhea. Our experience coincides with theirs that diarrheal deaths, when they occur, are "almost entirely restricted to severely malnourished infants." It was this observation which inspired our efforts to improve nutrition in this condition by early oral feeding.

Summary

Early oral feeding is recommended in infantile diarrhea not as a substitute but as a supplement to needed parenteral therapy. An analysis of pertinent data indicates the safety and value of this procedure.

References

1. Chung, A. W., Effect of oral feeding at different levels on absorption of foodstuffs in infantile diarrhea, J. Pediat. **33**:1, 1948.

2. Chung, A. W., and Viscorova, B., Effect of early oral feeding versus early oral starvation on course of infantile diarrhea, J. Pediat. **33**:14, 1948.
3. Warthen, R. O., Early oral feeding in treatment of infantile diarrhea, Clin. Proc. Child. Hosp. **5**:11, 1948.
4. O'Keefe, E. S., Enteral treatment of diarrhea in infancy, Am. J. Dis. Child. **76**:616, 1948.
5. Dancis, J., and others, Dehydration in infantile diarrhea, M. Clin. North America **33**:851, 1949.
6. Freudenberg, E., Ernährungstherapie im Säuglingsalter und Ernährungstherapeutischer Nihilismus, Ann. pædiat. **172**:308, 1949.
7. Darrow, D. C., and others, Disturbances of water and electrolyte metabolism in infantile diarrhea, PEDIATRICS **3**:129, 1949.

SPANISH ABSTRACT

Lugar de Alimento Oral en la Diarrea Infantil

Se recomienada la alimentación oral temprana en la diarrea infantil no como un substituto sino como un suplemento a la terapia parentérica necesitada. Un análisis de informes pertinentes indica la seguridad y valor de este procedimiento.

477 First Avenue

FURTHER OBSERVATIONS ON THE ABSORPTION OF VITAMIN A

Influence of the Particle Size of the Vehicle on the Absorption of Vitamin A

By J. M. LEWIS, M.D., SIDNEY Q. COHLAN, M.D., AND ANGELINA MESSINA, A.B.
New York City

CLIFFORD[1] reported that "aqueous" preparations of vitamin A brought about higher concentrations of vitamin A in the blood of premature infants than did the oily products. This same phenomenon was reported by Kramer, Sobel and Gottfried[2] in normal children and in patients with celiac disease and by Lewis, Bodansky, Cohlan and Birmingham[3] in normal infants, children and adults, as well as in cystic fibrosis of the pancreas and obstructive jaundice.

The significance of the higher blood levels following the administration of "aqueous" preparations of vitamin A was investigated in a previous study.[3] That these levels represented superior absorption of the "aqueous" preparation was indicated by the results of studies on fecal excretion. Thus, when the "aqueous" preparations were administered, only 7% of the vitamin A intake was excreted in the stools as compared with 38% following the administration of the oily product. Furthermore, in experiments on rats and guinea pigs we found, not only higher blood levels and lower fecal excretion of vitamin A following the administration of "aqueous" preparations, but also greater storage in the liver.

The "aqueous" preparations of vitamin A are not true solutions, but rather fine colloidal suspensions of oil containing vitamin A in an aqueous medium. This fine dispersion is due to the incorporation in these preparations of solubilizers, or tweens, and, when one examines them under high magnification, the particle size of the oil is so small that it is not visible. On the other hand, the particle size of the oily preparations of vitamin A is visible to the naked eye when mixed with water or intestinal contents. The studies of Frazer[4] on fat absorption suggest that the "aqueous" preparations owe their high degree of absorption of vitamin A to the minute particle size of the oil contained therein. The present investigation is concerned with the role of the particle size of the vehicle of vitamin A in the absorption of the vitamin from the intestinal tract.

In view of the fact that the vitamin A component of milk exists in the fat globules, the size of which varies from 0.5 to 10 μ depending upon whether the milk is homogenized or not, it was thought worth while to investigate the absorption of vitamin A as it occurs naturally in milk, and to compare it with the absorption of oily and "aqueous"

From the Department of Pediatrics, New York University College of Medicine, and from the Children's Medical Service of Bellevue Hospital and the Pediatric Service of Beth Israel Hospital, New York, N.Y.

Aided by grants from Mead Johnson Company, Evansville, Ind., and the Loyal League for Philanthropies, New York, N.Y.

Presented before the 59th Annual Meeting of the American Pediatric Society, Atlantic City, N.J., May 5, 1949.

(Received for publication June 30, 1949.)

preparations of vitamin A. Information of this kind would not only be of value in ascertaining the mechanism of vitamin A absorption, but would be of practical value, inasmuch as milk is the basic portion of the infant's diet.

Accordingly, four infants, ranging in age from 2 to 3 months, were given 20 ounces of milk daily, the vitamin A content (excluding the carotene value) of which was 450 units. Stools were collected for a period of four days and assayed for their vitamin A content by a method which was previously described.[3] During a second period of four days, an oily supplement containing 450 u. was given and during a third period, an

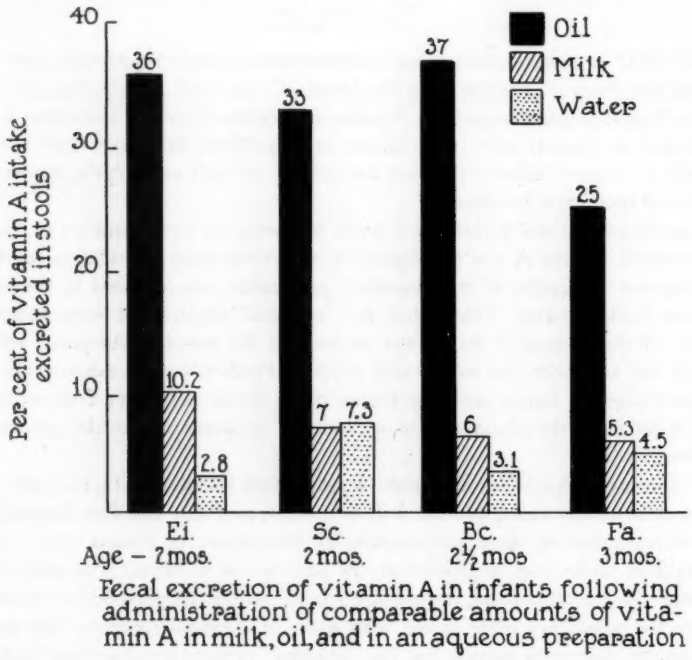


CHART 1. Fecal excretion of vitamin A in infants following administration of comparable amounts of vitamin A in milk, in oil and in "aqueous" preparation.

"aqueous" preparation containing the same number of units was added. Stools were similarly collected and analyzed for vitamin A. It may be added that during the oily and "aqueous" periods the infants received a total of 900 u. daily, as compared with an intake of 450 u. when the milk was the only source of vitamin A. We had attempted to use skimmed milk during the periods in which the supplements were administered in order to have the same intake of vitamin A for all three periods, but the babies developed diarrhea following the use of skimmed milk, and it was necessary to carry out the experiments in the aforementioned manner. The excretion of vitamin A resulting from the "aqueous" and oily preparations was determined by subtracting the basal excretion of vitamin A during the milk period from the total excretion during the periods when the supplements were given.

The results of this experiment appear in Chart 1, where it will be noted that the largest

fecal excretion of vitamin A occurred when the oily preparation was given and the smallest, when the "aqueous" preparation was administered. During the period when milk alone was fed, the excretion of vitamin A was considerably lower than when the oily preparation was given and slightly higher than when the "aqueous" preparation was fed. Thus, the average fecal excretion of vitamin A following the administration of milk was 7.1% of the intake, as compared with 32.7% and 4.4% during the oily and "aqueous" periods, respectively.

As previously stated, the vitamin A component of milk exists exclusively in the butter

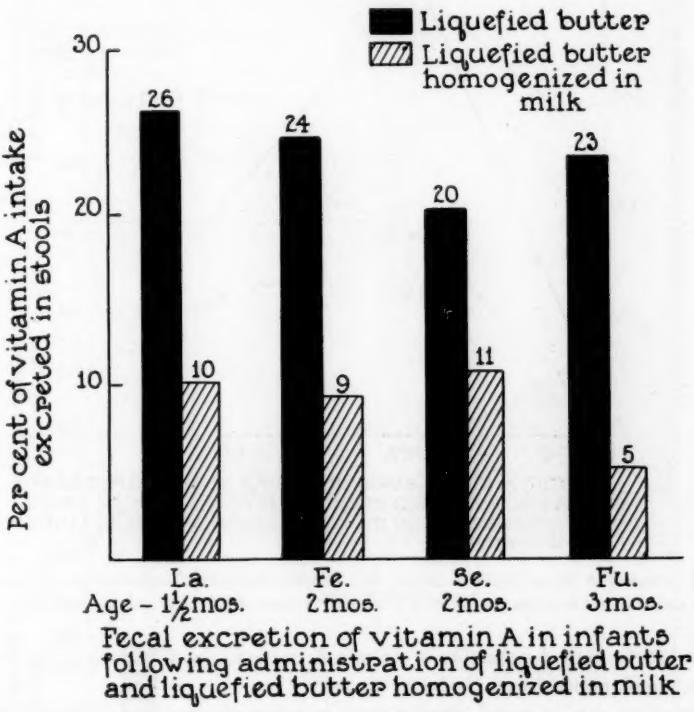


CHART 2. Fecal excretion of vitamin A in infants following administration of liquefied butter and liquefied butter homogenized in milk.

fat and the question arises whether the high absorbability of vitamin A in milk is due to the superior absorption of butter fat, or to the dispersion of butter fat globules in milk. In order to evaluate these possibilities, an experiment was carried out in which four young infants were given liquefied butter alone and, subsequently, liquefied butter homogenized in milk; a comparison of the vitamin A excretion was made following the use of these preparations. A hand homogenizer was used for emulsifying 15 cc. of melted butter into the morning and evening formulas. The administration of melted butter alone was carried out by gavage in 15 cc. amounts, twice daily. Assay of the butter revealed an average value of 15 u. of vitamin A/cc. The particle size of the butter homogenized in milk varied from 2 to 10 μ.

The results of this experiment are shown in Chart 2. It will be noted that in all four infants the excretion of vitamin A in the feces is considerably higher with the use of unemulsified butter as compared with the administration of butter emulsified in milk. Thus, the vitamin A excretion in the stools was 23.2% of the intake following liquefied butter, and only 8.7% following butter dispersed in milk by homogenization. It may be added that analyses of the stools for fat revealed that a considerably larger excretion of fat occurred when unemulsified butter was administered. These results would therefore

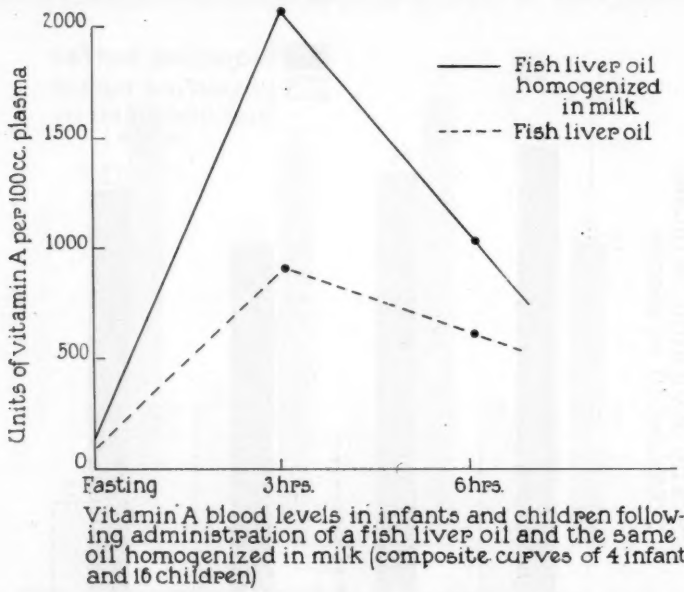

2000
1500
1000
500
0
Units of vitamin A per 100cc. plasma
Fasting
3 hrs.
6 hrs.
Fish liver oil homogenized in milk
Fish liver oil
Vitamin A blood levels in infants and children following administration of a fish liver oil and the same oil homogenized in milk (composite curves of 4 infants and 16 children)

CHART 3. Vitamin A blood levels in infants and children following administration of fish liver oil and same oil homogenized in milk (composite curves of 4 infants and 16 children).

indicate that the high absorbability of vitamin A is due to the dispersion of the butter fat globules in milk rather than to the butter fat itself.

The question may be raised whether fecal excretion of vitamin A is a good indicator of the absorption of the vitamin. In a previous communication,[3] it was shown that when the fecal excretion of vitamin A was high following a test dose of the oily preparation, the vitamin A levels in the blood were low, and, conversely, when the vitamin A excretion was low following the "aqueous" preparation, the vitamin A concentrations in the blood were high. Thus, it would seem that fecal excretion of vitamin A is a good criterion of the absorption of the vitamin. Unfortunately, the vitamin A content of milk is not high enough to bring about significant elevations in the concentrations of vitamin A in the blood, and a direct comparison of the vitamin A blood levels following the administration of milk, oily and "aqueous" preparations was not possible. However, if one augments the vitamin A content of milk by homogenizing a fish liver oil preparation into the milk, one can study the effect on blood levels of the reduction in particle size of the vehicle. We therefore decided to compare the blood levels following the administration of a fish

liver oil homogenized in milk, and a fish liver oil administered in the usual manner. For this experiment oleum percomorphum was homogenized in milk at a pressure of 5,000 pounds per square inch.* The average size of the oleum percomorphum globule, as a result of homogenization, was 1 to 2 μ and the potency of the fortified milk was 2,500 u. of vitamin A/cc.

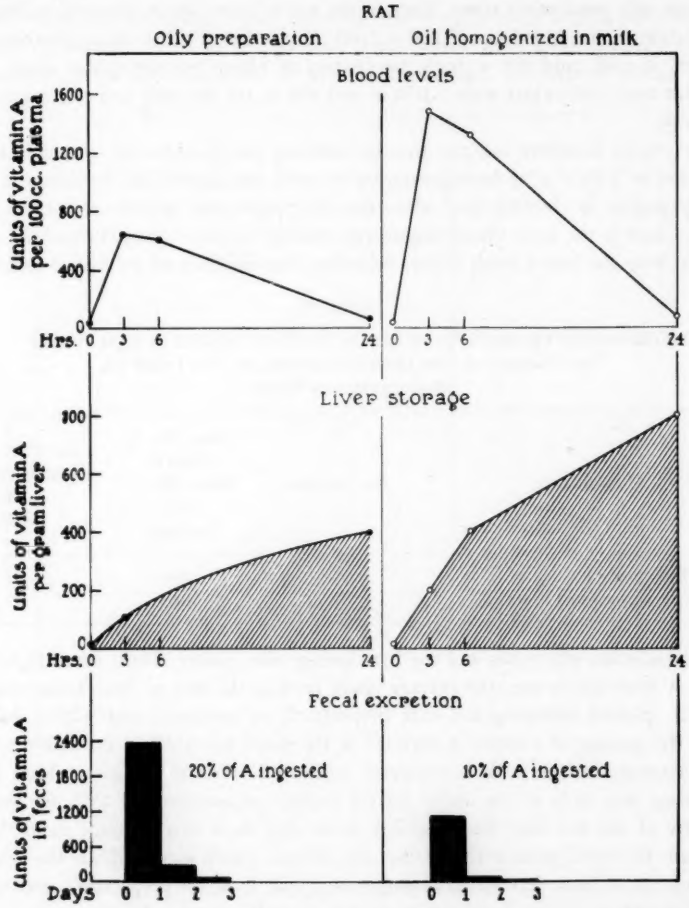


CHART 4. Vitamin A blood levels, liver storage and fecal excretion in rats receiving fish liver oil and same oil homogenized in milk.

Sixteen children, from 5 to 12 years of age, and four infants were given vitamin A 5,000 u./pound body weight of the oleum percomorphum emulsified in milk. The concentration of vitamin A in the blood was determined 3 and 6 hours following the administration of the fortified milk. Several days later a comparable number of units of

* Acknowledgment is made to Sheffield Farms for their cooperation in the preparation of the fortified milk.

oleum percomorphum alone was administered and blood samples were similarly obtained for vitamin A analyses.

The results of this experiment are illustrated in Chart 3, where it will be noted that significantly higher blood levels were found following the administration of the oily preparation homogenized in milk as compared with those obtained with the administration of the oily preparation alone. Thus, at the end of three hours, the average vitamin A concentration in the blood was 2,100 u./100 cc. plasma with the oleum percomorphum emulsified in milk, and 850 u. with the feeding of oleum percomorphum alone. At the end of six hours the values were 1,050 u. and 650 u. for the milk and oily preparations, respectively.

These results therefore indicate that by reducing the particle size of a fish liver oil preparation to 1 to 2 μ by homogenization in milk, the absorption of vitamin A is considerably greater in children than when the oily preparation is given alone. As is indicated in Chart 4, the same phenomenon was observed in experiments carried out on rats. Not only were the blood levels higher following the fish liver oil emulsified in milk, but

TABLE I

COMPARATIVE VITAMIN A BLOOD LEVELS AND LIVER STORAGE IN RATS FOLLOWING FEEDING OF FISH LIVER OIL ALONE AND FISH LIVER OIL HOMOGENIZED IN WATER

Preparation	No. Animals	Conc. Vit. A Units in Blood/100 cc. 3 Hr. (Average)	Per Cent Vit. A Intake Stored in Liver 24 Hr.
Fish liver oil	13	600	23
Oil homogenized in water	13	1040	41

the fecal excretion was lower and the liver storage was greater. Thus, when 13,000 u. of vitamin A were fed to rats, the average blood level at the end of three hours was 1,480 u./100 cc. plasma following the milk preparation, as compared with 620 u. following the oil; the amount of vitamin A excreted in the stools was 10% of the intake when the oil was homogenized in milk as compared with 20% when it was given alone, and the liver storage was 46% of the intake for the former preparation and 23% for the latter.

In view of the fact that the possibility exists that there may be some factor in milk, apart from the small particle size of the oily globule, which may facilitate the absorption of vitamin A, it was decided to homogenize a fish liver oil preparation into water to ascertain whether improved absorption would also take place under these circumstances. Accordingly, oleum percomorphum was emulsified in water using the same homogenizer as was employed for its homogenization into milk. This emulsion was quite stable for a period of 12 to 24 hours and the particle size of the oily globule was 1 to 2 μ during the first 12 hours after homogenization. Later they became larger and coalesced and the oil separated out. Rats were fed 13,000 u. of this preparation within 12 hours after it was prepared and a control group was given oleum percomorphum alone. The effect of these preparations on the vitamin A concentration in the blood and on liver storage will be noted in Table I. It will be observed that the blood level was significantly higher, and the liver storage greater, when the rats were fed the oil emulsified in water. Thus, the en-

hanced absorption of vitamin A following the administration of the fish liver oil preparation homogenized in milk must be attributed to the small particle size of the oily globule rather than to any factor in the milk itself.

Part Two

In the first part of this paper it was demonstrated that, by reducing the particle size of the vehicle of vitamin A to 1 to 2 μ, whether it was butter fat or a fish liver oil, a significant enhancement in the absorption of vitamin A resulted. In order to obtain further

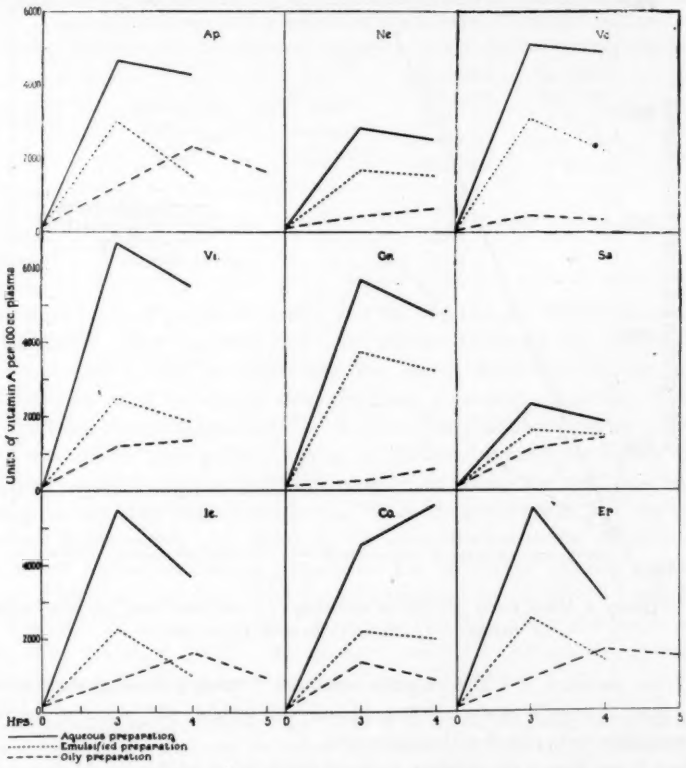


Chart 5. Vitamin A blood levels in children following administration of oily, emulsified and "aqueous" preparations of vitamin A.

information on the relationship of particle size to vitamin A absorption, it was decided to compare the absorption of various proprietary emulsions with that of the so-called "aqueous" preparations. The particle size of the oil contained in the emulsion varied from 1 to 20 μ whereas, as previously stated, the particle size of the "aqueous" preparations is so small that it cannot be seen under high power magnification and for practical purposes may be regarded as submicroscopic. If the thesis were correct, that the particle size of the vehicle of the vitamin A affects its absorption, one would expect, *a priori,* that the "aqueous" preparations would be absorbed to a higher degree than the emulsions.

The emulsions were cloudy, and the oil was held in suspension by a gummy agent, such

as tragacanth. The "aqueous" preparations were clear because of the fine colloidal dispersion of the oily droplets due to the use of solubilizers, such as mannitan or sorbitan monolaurate. Two of the three emulsions and two of the three "aqueous" preparations employed in this investigation contained the vitamin A ester, whereas, the third emulsion and the third "aqueous" preparation contained the vitamin A alcohol.

Eleven children, 6 to 12 years of age, were given an "aqueous," an emulsified and an oily preparation of vitamin A* at intervals of 3 to 4 days, and blood for vitamin A

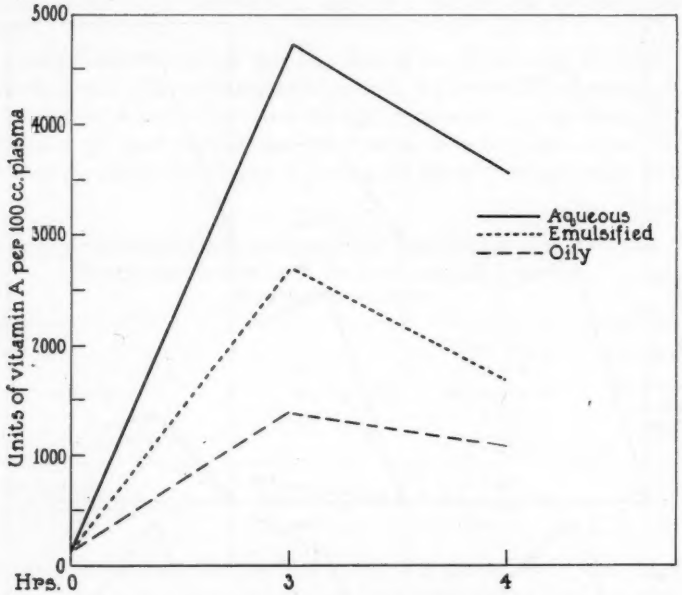


CHART 6. Vitamin A blood levels in children receiving oily, emulsified and "aqueous" preparations of vitamin A (composite curves of 11 children).

analyses were obtained 3, 4 and, in some instances, 5 hours following their administration. The dose of vitamin A was 5,000 u./pound body weight; the "aqueous" preparations and the emulsions were mixed with tomato juice.

In Chart 5 are shown the vitamin A blood levels for 9 of the 11 children following the use of the three preparations of vitamin A. It will be observed that in all nine instances, the blood levels were highest following the "aqueous" preparation, intermediate, following the emulsions and lowest, following the oily product. The average vitamin A values obtained in the 11 children following the administration of the three types of preparation is plotted in Chart 6. At the end of three hours the average concentration of vitamin A in the blood was 4,700 u./100 cc. plasma for the "aqueous" preparation, 2,600 u. for the emulsion and 1,200 u. for the oily product, whereas, at the end of four

* The "aqueous" preparations used in this study were Poly-Sol (Mead Johnson), ViPenta (Hoffman-LaRoche) and Vi-Syneral (U. S. Vitamin Corporation). The emulsions were Poly-Vitamin Dispersion (Mead Johnson), Laboratory Product #257 (Mead Johnson) and Multi-Vitamin Emulsion (Scott & Bowne). The Poly-Sol, ViPenta, Laboratory Product #257 and Poly-Vitamin Dispersion contain a vitamin A ester, whereas the other products contain vitamin A alcohol.

hours the values were 3,600 u., 1,750 u. and 1,050 u. for the "aqueous," emulsion and oily preparations, respectively.

Thus, the preparation with the smallest particle size of the vitamin A vehicle ("aqueous") brought about the highest blood levels, those with the larger particle size (emulsion) brought about intermediate values, whereas, those with the largest particle size (oil) resulted in the lowest elevations of vitamin A concentration in the blood.*

TABLE II

RELATIONSHIP OF PARTICLE SIZE OF VEHICLE OF VITAMIN A TO CONCENTRATION OF VITAMIN A IN BLOOD, TO LIVER STORAGE AND TO FECAL EXCRETION IN RATS

Preparation	Particle Size (Microns)	No. Animals	Average Blood Level 3 Hr. U./100 cc. Plasma	Average Per Cent Vit. A Intake Stored in Liver	Average Per Cent Vit. A Intake Excreted in Feces
Fish liver oil	Macroscopic	48	620	25	20
Emulsion	1–20	70	1370	38	12
"Aqueous"	Submicroscopic	48	2370	50	7

These three types of preparations were also fed to rats and a comparison was made of the blood levels, fecal excretion and liver storage following the administration of vitamin A 13,000 u. For this experiment 166 animals were used and the results will be published in detail in another communication. However, a summary of the results appears in Table II. It will be noted that the blood levels following the use of these preparations were of the same order in rats as in children, namely, the highest values following the "aqueous" preparations, intermediate, following the emulsions and lowest, following the oily. The fecal excretion was 7% of the intake when the "aqueous" preparation was administered, 12% following the administration of the emulsion and 20% following the feeding of the oily preparation. The amount of vitamin A stored in the livers is in complete agreement with the data obtained on vitamin A blood levels and fecal excretions. Thus, the "aqueous" preparation brought about the largest storage of vitamin A in the livers (50%), the emulsion resulted in intermediate stores (38%), and the oily product brought about the lowest storage (25%).†

* It may be added that no difference was found in the absorption among the 3 "aqueous" preparations. Similarly, the 3 emulsions showed no difference in their absorption. Thus, the vitamin A alcohol and the vitamin A ester were absorbed to the same degree in each of the 2 types of vitamin A preparations.

† The question has been raised whether the solubilizer, or tween, in the "aqueous" preparation facilitates the absorption of vitamin A by direct action on the intestinal mucosa. If such were the case, then the superior absorption of vitamin A in the "aqueous" preparation could not be attributed entirely to the small particle size of the vehicle. It was therefore thought worth-while to administer simultaneously a fish liver oil preparation and a solubilizer (tween 80) to ascertain whether the presence of tween in the intestinal tract would enhance the absorption of the vitamin A contained in the fish liver oil preparation. This experiment was carried out on 6 children and 30 rats. The results revealed that the addition of tween brought about no higher blood levels than when the fish liver oil preparation was fed alone. Furthermore, the liver storage and fecal excretion in rats were not affected by the administration of the tween. These findings would indicate that the solubilizer, or tween, does not aid in the absorption of vitamin A by a direct action on the intestinal mucosa, but is of value only in maintaining the minute particle size of the vitamin A concentrate in the "aqueous" preparations.

In a previous communication we reported that the "aqueous" preparation of vitamin A brought about a normal absorption curve in the blood of a child with cystic fibrosis of the pancreas. May and Lowe[5] showed that the administration of vitamin A emulsions, the average particle size of which ranged from 0.5 to 10 μ, also resulted in satisfactory elevations in the concentration of vitamin A in the blood in cystic fibrosis of the pancreas. It was thought worth while to compare the absorption of the three types of vitamin A preparations in a 2 year old child having this disease. The results are revealed in Table III and indicate that, under conditions of impaired fat absorption, the degree of absorption of vitamin A is also dependent upon the particle size of the vehicle. Thus, the "aqueous"

TABLE III

RELATIONSHIP OF PARTICLE SIZE OF VEHICLE OF VITAMIN A TO CONCENTRATION OF VITAMIN A IN BLOOD OF 2 YEAR OLD CHILD WITH CYSTIC FIBROSIS OF PANCREAS

Preparation	Particle Size (Microns)	Maximum Blood Rise (U./100 cc. Plasma)
Fish liver oil	Macroscopic	36
Emulsion	1–2	500
"Aqueous"	Submicroscopic	940

preparations brought about the highest rise in the vitamin A concentration in the blood, namely, 940 u./100 cc. plasma, the emulsion resulted in a rise of 500 u., whereas, as was expected, the oil brought about almost no rise. It may be added that the emulsion and the "aqueous" preparation used for these tests contained the vitamin A ester.

DISCUSSION

The results of this investigation demonstrate the relationship of particle size of the vehicle of vitamin A to intestinal absorption. The "aqueous" preparations owe their superior absorption to the minute particle size of the oil contained therein. The emulsions containing oily droplets varying from 1 to 20 μ were not quite as effectively absorbed as the "aqueous" preparations but were definitely superior to the oily products.*

These findings are in accord with the studies of Frazer[4] who showed that fats are absorbed in particle form irrespective of lipolysis. He has demonstrated that the triglyceride of fat is finely dispersed in the intestinal lumen into minute particles of less than 0.5 μ in diameter which pass through the intestinal cell without necessarily undergoing hydrolysis. The importance of particle absorption is demonstrated in experiments carried out with paraffins. When they are administered as a crude oil no absorption occurs. If, however, they are mechanically emulsified so that the particles are less than 0.5 μ in diameter they may be absorbed to the same degree as an olive oil emulsion.

* In a recent communication, McCoord and her co-workers[6] reported that an oily concentrate of high vitamin A potency, 210,000 u./cc., brought about vitamin A blood levels almost as high as those which resulted from the administration of an "aqueous" preparation of vitamin A. In view of the fact that this finding did not seem to be consistent with the implications of our study, we carried out absorption tests on 10 children using the same oily concentrate they employed (Abbott). Contrary to their observations, we found that the administration of this oily vitamin A concentrate resulted in much lower vitamin A blood levels than those which occurred following the use of an "aqueous" preparation. Thus, the average maximum rise was 1,400 u./100 cc. plasma following the oily concentrate as compared with 4,500 u. following the "aqueous" preparation.

The data which we obtained in a child with cystic fibrosis of the pancreas would indicate that hydrolysis of the vitamin A ester is not necessary for the absorption of vitamin A. With the administration of the fish liver oil preparation no absorption took place, presumably because the absence of pancreatic esterases and lipases in this condition did not permit hydrolysis of the vitamin A ester or fat with a consequent reduction in particle size. On the other hand, when the particle size of the oil was reduced to 1 to 2 μ, or to submicroscopic proportions, the vitamin A esters contained in these preparations were well absorbed in spite of the absence of pancreatic lipases or esterases.

Recent reports[7-9] indicate that there is an increase in the incidence of hypervitaminosis A. In most instances over-zealous mothers have fed their infants one to two teaspoonfuls of an oily preparation of vitamin A containing 50,000 u./cc. for a period of months. Inasmuch as the "aqueous" preparations of vitamin A are more potent, unit for unit, than the oily preparations, and, in view of the probability that the "aqueous" preparations will be used more widely in the future, efforts must be made to prevent further overdosage of vitamin A. In most of the cases of hypervitaminosis A reported, mothers have purchased bottles containing 50 cc. of the highly potent oily preparation. We would therefore recommend that the size of the bottles containing vitamin A should be no larger than 15 cc., as a mother cannot administer excessive amounts of the preparation when the capacity of the bottle is about three teaspoonfuls. Furthermore, the potency of vitamin A preparations should be no greater than 10,000 u./cc. Under these conditions it will be most unlikely for hypervitaminosis A to take place.

Summary

Experiments carried out on infants revealed that vitamin A, as it occurs naturally in milk, was more effectively absorbed than when administered in an oily vehicle, but not quite as well absorbed as when given in an "aqueous" preparation. The high degree of absorbability of vitamin A in milk is due to the relatively small particle size of the butter fat globule.

By reducing the particle size of a fish liver oil preparation (oleum percomorphum) to 1 to 2 μ by homogenization into milk or water, the absorption of vitamin A was considerably enhanced in children and in rats.

The relationship of the particle size of the vehicle of vitamin A to absorption is further demonstrated by the results of the administration in children and in rats of three vitamin A preparations of varying particle size. Thus, the highest absorption occurred following the administration of a preparation containing particle size of submicroscopic proportion ("aqueous"); the lowest absorption resulted following the preparation containing particles macroscopic in size (oil) and intermediate absorption was observed following the use of a preparation containing particle sizes varying from 1 to 20 μ (emulsion).

Similarly, in a child having cystic fibrosis of the pancreas, the absorption of vitamin A was dependent upon the particle size of the vehicle employed.

References

1. Clifford, S., Vitamin A absorption in premature infants, Society for Pediatric Research, Skytop, Pa., May 1946.
2. Kramer, B., Sobel, A. E., and Gottfried, S. P., Serum levels of vitamin A in children, Am. J. Dis. Child. **73**:543, 1947.
3. Lewis, J. M., Bodansky, O., Birmingham, J., and Cohlan, S. Q., Comparative absorption, excretion and storage of oily and aqueous preparations of vitamin A, J. Pediat. **31**:496, 1947.

4. Frazer, A. C., Metabolism of fat, J. Roy. Soc. Arts **96**:582, 1948.
5. May, C. P., and Lowe, C. U., Absorption of orally administered emulsified lipid in normal children and in children with steatorrhea, J. Clin. Investigation **27**:226, 1948.
6. McCoord, Augusta B., and others, Absorption of oily and aqueous preparations of ester and alcohol vitamin A by normal children and children with various diseases, PEDIATRICS **2**:652, 1948.
7. Joseph, H. W., Hypervitaminosis A and carotinemia, Am. J. Dis. Child. **67**:33, 1944.
8. Toomey, J. A., and Morissetta, R. A., Hypervitaminosis A, Am. J. Dis. Child. **73**:473, 1947.
9. Caffey, J., Vitamin A poisoning, American Pediatric Society, Atlantic City, N.J., May 1949.

SPANISH ABSTRACT

Otras Observaciones sobre la Absorción de la Vitamina A; Influencia del Tamaño de la Partícula del Vehículo en la Absorción de la Vitamina A

Los experimentos llevados a cabo en infantes revelaron que la vitamina A, como ocurre naturalmente en leche, fué absorbida más eficazmente que cuando administrada en un vehículo aceitoso; pero no tan bien absorbida como cuando dada en una preparación "acuosa." El alto grado de absorbabilidad de la vitamina A en leche es debido al tamaño de la partícula relativamente pequeño del glóbulo de grasa de mantequilla.

Reduciendo el tamaño de la partícula de una preparación de aceite de higado de pesacado (Oleum percomorphum) a 1 a 2 μ mediante homogenización en leche o agua, la absorción de la vitamina A fué considerablemente aumentada en niño y en ratas.

La relación del tamaño de la partícula del vehículo de la vitamina A con la absorción está además demostrada por los resultados de la administración en niños y en ratas de tres preparaciones de vitamina A de diferente tamaño de partícula. Así, la absorción más alta ocurrió después de la administración de una preparación conteniendo un tamaño de particula de proporción submicroscópica ("acuosa"); la absorción más baja resultón después de la preparación conteniendo partículas microscópicas en tamaño (aceite) y la absorción intermedia se observó después del uso de una preparación conteniendo tamaños de partículas variando de 1 a 20 μ (emulsión).

Similarmente, en un niño con fibrosis cística del pancreas, la absorción de la vitamina A dependió del tamaño de partícula del vehículo empleado.

25 East 83rd Street

SUCCESSFUL TREATMENT OF C. DIPHTHERIAE SUBACUTE BACTERIAL ENDOCARDITIS WITH PENICILLIN AND STREPTOMYCIN

By JOHN R. ALMKLOV, M.D., AND ARILD E. HANSEN, M.D., PH.D.
Galveston

FINDING C. diphtheriae as the causative organism in subacute bacterial endocarditis is unusual. Only 17 cases have been reported and none has survived. The successful treatment of an 8 year old child with the combined use of penicillin and streptomycin warrants presentation of the case and affords an opportunity to discuss the possible therapy of choice in such a condition.

Howard[1] in Baltimore, in 1893, reported the first case of subacute bacterial endocarditis due to C. diphtheriae. Pertinent data concerning the 17 reported cases of this condition are summarized on Table I. Diagnosis was proven by positive culture either from the blood stream during life or from the heart at autopsy. All but three of these have been recorded in the European literature. In nine instances the disease followed nasopharyngeal diphtheria. Eleven of the patients were children. According to the standard guinea pig virulence test, seven of the patients succumbed to avirulent strains of C. diphtheriae. At autopsy the mitral valve was found to be involved in 12 instances, the tricuspid in 5, and the aortic in 3, while four patients were found to have multiple valvular disease. Only three had a history of previous rheumatic fever. Most of the patients had received large doses of diphtheria antitoxin; however, some had no specific therapy. None had been treated with antibiotic agents. A rather rapid downhill course typified each case and all succumbed to the effects of the bacterial invader.

CASE REPORT

B. D., an 8 yr. old white female, entered the Children's Hospital of the University of Texas. Present illness started 3 wk. earlier when she developed an upper respiratory infection. Four days later she had a shaking chill followed by a high fever. Because the temperature remained elevated during the next 3 days the family physician prescribed both penicillin and sulfadiazine. At this time the patient complained of abdominal pain and had anorexia. Fever continued but the abdominal pain subsided. On the 12th day of illness she complained of pain in her right heel. There was no heat, tenderness, swelling or limitation of motion of the affected joint. The pain shifted next to the right knee and then to the left knee. There was a weight loss of 2.25 kg. during the 3 wk. preceding her admission to the hospital.

Her past history is significant in that at 4 yr. of age she had tonsillitis followed by joint pains. A heart murmur was detected and with the assistance of electrocardiographic and roentgenologic examination her physician made the diagnosis of rheumatic heart disease. It is also pertinent that in several examinations prior to this illness, her physician had not reported the presence of a murmur. There was no history of rheumatic fever in the family. The patient was immunized for diphtheria when she was an infant, but the mother did not know whether the subsequent Schick test was positive or negative.

Physical examination revealed a chronically ill, pale, listless child who appeared fairly well nourished. Blood pressure 90/60 mmHg., pulse 102/min., respiration 20/min., temperature 39.7° C. Nose and throat were clear. There were a few moist rales at the base of the right lung posteriorly.

The Department of Pediatrics, University of Texas School of Medicine, Galveston, Texas.
(Received for publication July 6, 1949.)

TABLE I

DATA CONCERNING 17 RECORDED CASES OF SUBACUTE BACTERIAL ENDOCARDITIS CAUSED BY C. DIPHTHERIAE

Case No.	Authors	Age Yr.	Sex	Naso-pharyngeal Diphtheria	Culture for C. Diphtheriae			Valvular Involvement at Autopsy
					Pre-mortem from Blood	Post-mortem from Heart	Virulence (Guinea Pig)	
1	Howard[1] 1893	44	M	None	—	Pos.	Neg.	Mitral and Aortic
2	Roosen-Runge[2] 1903	19	M	None	Pos.	Pos.	Neg.	Tricuspid and Aortic
3	Herzog[3] 1918	7	M	None	—	Pos.	Pos.	Mitral
4	Roosen-Runge[4] 1925	2	F	None	Pos.	Pos.	Neg.	Tricuspid
5	Chiari[5] 1933	6	F	Yes	—	Pos.	Pos.	Tricuspid
6	Chiari[6] 1935	10	F	Yes	—	Pos.	Pos.	Mitral
7	Sutherland and Willis[7] 1936	18	M	None	Pos.	—	Neg.	Mitral
8	Jedlička[8] 1936	10	F	Yes	Neg.	Pos.	Pos.	Mitral
9	Same	8	M	Yes	Pos.	Pos.	Pos.	Mitral
10	Same	9	M	Yes	Pos.	Pos.	Pos.	None (mural thrombus left ventricle)
11	Same	4	F	Yes	Pos.	Pos.	Pos.	Tricuspid and Mitral
12	Buddingh and Anderson[9] 1937	16	M	None	Pos.	Pos.	Pos.	Mitral
13	Lenti and Wirz[10] 1938	45	F	Yes	Pos.	—	Pos.	Mitral
14	Kaschel[11] 1938	9	F	Yes	Pos.	Pos.	Neg.	Mitral
15	Wallner[12] 1939	56	M	None	Pos.	—	Neg.	Aortic and Tricuspid
16	Galambos[13] 1941	5	F	Yes	—	Pos.	Pos.	Mitral
17	Pull[14] 1946	10	F	None	Pos.	—	Neg.	Mitral

Left border of cardiac dullness was 2 cm. outside the midclavicular line. Apical impulse was in the 6th ICS. There was a loud, harsh murmur heard throughout systole, loudest at the apex. A faint diastolic murmur was also present at the apex. Rhythm was regular and the tones were of fair quality. The liver was palpated 3 cm. below the costal margin and was slightly tender. The spleen was not palpable. The patient complained of pain in the left knee but no objective evidence of disease was found on examination. There were no petechiae. The rest of the physical examination disclosed no abnormalities.

Laboratory examination: Hgb. 10 gm./100 cc.; RBC, 2.3 million; WBC, 7.6 thousand with 75% neutrophiles; corrected ESR (Wintrobe) 28 mm. in 1 hr.; antistreptolysin titre, 50 u./cc.; tuberculin test 1:1000 OT, negative; Schick test, negative; Kahn, negative; fasting blood glucose, 105

mg./100 cc.; and repeated urinalysis, negative except for albuminuria during febrile episodes.

Bacteriologic studies of the nose and throat revealed alpha streptococci but were negative for C. diphtheriae. Blood culture on admission revealed a pure culture of C. diphtheriae. Two days later, the blood culture was again positive for the same organism. Because of the unusual nature of the bacteria, isolated from the blood stream, special studies were made. All the bacteriologic characteristics of C. diphtheriae were found and it was classified as an intermedius strain. The virulence test was positive when the organism was injected into guinea pigs.

ECG taken 3 days after admission revealed a rate of 105/min.; P-R interval, 0.17 sec.; low T wave in lead I, and a negative T wave in lead IV F. Fluoroscopy of the heart demonstrated enlargement of the R and L ventricle. There also was a slight enlargement of the L auricle.

Course in hospital: The nature of the course of the illness may be followed in Chart 1. Because of the positive blood culture on the 3rd day of admission, penicillin, 200,000 u. every 3 hr. intra-

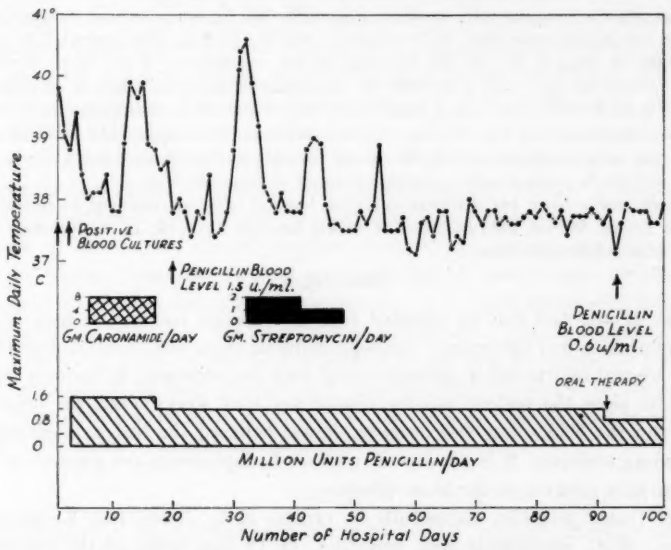


CHART 1. Course of disease in 8 yr. old girl with subacute bacterial endocarditis caused by C. diphtheriae.

muscularly were exhibited. The next day the patient complained of pain in her right elbow but examination of the joint was not remarkable. The joint pain did not respond to salicylate therapy. Caronamide was given for a period of 11 days starting 4 days later, the dose being 1.4 gm. every 4 hr. for a total of 92.4 gm. On the 14th day of admission the patient complained of severe pain in her right chest and developed a rise in temperature to 40° C. Venous pressure was 18.5 cm. of saline. Roentgenographic examination of the chest revealed evidence of an infarction in the right lower lobe.

One month after admission the patient developed a temperature of 40.6° C. and became stuporous. Her condition was extremely critical. Sensitivity tests on the organism which were carried on during this interval revealed: penicillin sensitivity, 0.05 u./ml.; streptomycin, 3.0 u./ml.; and Na-sulfadiazine, 5.0 mg./100 ml. Because the patient had failed to respond to penicillin alone and because the organism was fairly sensitive to streptomycin, it was decided to employ this drug as well as the penicillin. Streptomycin was given intramuscularly, 0.5 gm. every 6 hr. Improvement was dramatic following exhibition of the streptomycin. Nine days later the dose was reduced to one half and the drug was discontinued after 23 gm. had been given during a 16 day period. The patient remained essentially afebrile but penicillin was continued. A total of 75,200,000 u. was given parenterally during a 3 mo. period. The intramuscular penicillin maintained a blood level

of 1.5 u./ml. In addition to the penicillin therapy, because of marked cardiac failure, the patient was on a low salt diet. Intranasal oxygen was administered for 45 days. Supportive therapy also included xanthine and mercurial diuretics and 7 blood transfusions.

The patient continued to improve and remained afebrile. Her course was uneventful except that 3 mo. after admission she developed an abscess of the buttocks. This influenced the staff physician to prescribe oral penicillin. The dosage of oral penicillin employed was 800,000 u./day and was given for a 2 mo. period for a total of 55,200,000 u. This dose sustained a blood level of 0.6 u./ml. The abscess was incised and drained. The culture of the purulent material was sterile. She was discharged from the hospital 6 wk. later with the recommendation that oral penicillin be continued. There had been 20 consecutive negative blood cultures.

Second hospital admission: Two weeks after discharge, because of the return of the inflammation in her buttocks she was readmitted to the hospital. Physical examination revealed an alert, active, happy child. A harsh systolic murmur over the entire precordium, loudest at the apex, as well as a faint apical diastolic murmur were readily elicited. The left border of cardiac dullness was 1 cm. outside the left midclavicular line. ECG revealed a rate of 105/min.; P-R interval, 0.16 sec., and a diphasic QRS in leads I, II, and III. Roentgenographic examination of the heart showed distinct reduction in size but there was a moderate R ventricular enlargement, slight L auricular enlargement, and some L ventricular enlargement. There was a prominent pulmonary conus. When the patient was discharged on the 8th day, the induration in the buttocks had resolved. The oral penicillin was stopped and the patient was placed on sulfadiazine 0.5 gm. twice a day as a prophylactic measure for the prevention of a possible recurrence of rheumatic fever.

Follow-up study: Since her discharge from the hospital, she has continued to remain well and has gained 2.5 kg. She has been examined at weekly intervals for 6 wk. in the outpatient clinic and has had normal sedimentation rate.

Discussion

In view of the fact that all reported cases of subacute bacterial endocarditis caused by C. diphtheriae had succumbed, although many of them had received diphtheria antitoxin, it seemed logical not to attempt a trial with this substance as the only therapeutic agent. Also since the patient had the disease for four weeks when the organism was isolated and the Schick test was negative, it was believed she had an adequate amount of circulating antitoxin. It is not known whether C. diphtheriae can produce toxin when this organism is growing on the heart valves.

Skinner[15] used penicillin successfully on carriers of C. diphtheriae. Karelitz[16] treated 80 carriers of C. diphtheriae with penicillin. In 15 days 95% of the patients had a negative culture. This prompted the decision to give our patient penicillin. The sensitivity test of the organism to penicillin was 0.05 u./ml., justifying the choice of this drug. Hewitt[17] studied 21 strains of C. diptheriae and found a penicillin sensitivity range from 0.02 to 0.3 μg./ml. Therefore, the sensitivity of this child's organisms was within the usual range for nasopharyngeal strains of C. diphtheriae.

In spite of the daily administration of 1.2 million units of penicillin the patient's course in the hospital continued to be stormy. She was in variable degrees of cardiac failure. Even after four weeks of penicillin therapy the patient went into marked failure; her temperature rose to 40.6° C. and she became comatosed. No precedence for the use of streptomycin in such a condition could be found, but with a sensitivity of 3 u./ml., it was felt justifiable to use this antibiotic. The response to the added streptomycin was dramatic.

The *in vivo* observation of marked clinical improvement following the use of streptomycin seems to substantiate the findings of Hewitt[17] in experimental animals. He tested the sensitivity to streptomycin of seven strains of C. diphtheriae and the range was 1.0 to 3.0 μg./ml. He found that streptomycin given 15 minutes before an injection of

C. diphtheriae to guinea pigs and repeated three times at two hour intervals was much more effective than penicillin in saving the animals. The same dosage of penicillin and streptomycin was employed even though the *in vitro* sensitivity of the organism to penicillin was greater than to streptomycin.

Because of the experiments of Lankford and Lacey[18] demonstrating that *in vitro* combinations of antibiotics, especially aureomycin and penicillin, could antagonize each other in their effect on staphylococci, it was decided to test our organism in the same manner. One drop of 1:1000 dilution of an 18 hour culture of the C. diphtheriae from the patient's blood was placed in beef infusion broth and turbidimetric readings on a Klett-Summerson photometer were made after 18 hours. Streptomycin in nine concentrations varying from 0 to 3.0 μg./ml. was combined with aureomycin in nine different concentrations varying from 0 to 0.03 μg./ml. making a total of 81 combinations. This experiment was repeated with combinations of streptomycin and penicillin, aureomycin and penicillin, penicillin and streptomycin, aureomycin and sodium sulfadiazine, and penicillin and sodium sulfadiazine. The results on this organism of the combinations of antibiotics was an additive effect but there was no evidence of either synergism or antagonism.

This phase of the study is being continued by Miss Oleta Beck who is making similar determinations on strains of C. diphtheriae isolated from the throats of hospital patients with clinical diphtheria and also with standard strains of C. diphtheriae.

In view of the marked clinical response noted in our patient, the animal tests performed by Hewitt,[17] and his *in vitro* sensitivity tests, it would seem advisable to treat future cases of subacute bacterial endocarditis due to C. diphtheriae with a combination of large doses of penicillin and streptomycin as soon as a positive blood culture is obtained. The combination of the two antibiotics would tend to reduce the possibility of the organism becoming drug resistant. Of course *in vitro* sensitivity test should be done on the organism as soon as it is isolated so the clinician may be able to ascertain the blood level necessary to combat the infectious agent.

Summary

C. diphtheriae is an unusual causative organism in subacute bacterial endocarditis as only 17 cases have been recorded and none of these has survived. The 8 year old girl in this report is the first patient to have recovered. This child had two positive blood cultures for virulent intermedius strain of C. diphtheriae which was sensitive to 0.05 u./ml. of penicillin and to 3.0 u./ml. of streptomycin. The patient received penicillin therapy for one month and responded poorly. When streptomycin was also administered there was dramatic improvement. This clinical experiment tends to substantiate Hewitt's[17] work in animals which demonstrates that streptomycin is much more effective than penicillin in saving guinea pigs injected with C. diphtheriae. *In vitro* tests with the organism isolated in this patient revealed neither evidence of synergism nor antagonism when studied with combinations of penicillin, streptomycin, sodium sulfadiazine and aureomycin. It is suggested in future cases that a combination of penicillin and streptomycin be used and that sensitivity tests be performed on the organism so that the physician may determine the proper dosage of antibiotic.

References

1. Howard, W. T., Acute ulcerative endocarditis due to bacillus diphtheriae, Bull. Johns Hopkins Hosp. 4:32, 1893.

2. Roosen-Runge, Ein fall von diphtheriebazillensepsis, München. med. Wchnschr. **50**:1252, 1903.
3. Herzog, G., Demonstration einer ulzerösen endokarditis durch diphtheriebazillen, München. med. Wchnschr. **65**:29, 1918.
4. Roosen-Runge, Über bakteriänie durch diphtheriebacillen, Virchows Arch. f. path. Anat. **254**:379, 1925.
5. Chiari, H., Zur frage der diphtherie-endokarditis, Centralbl. f. allg. Path. u. path. Anat. **58**:193, 1933.
6. Chiari, H., Zur frage des uebertretens der diphtheriebazillen in die blutbahn und ihrer ansiedlung in inneren organen, Wien. klin. Wchnschr. **48**:685, 1935.
7. Sutherland, J., and Willis, R. A., Case of endocarditis due to diphtheroid bacillus structurally and culturally resembling diphtheria bacillus, J. Path. & Bact. **43**:127, 1936.
8. Jedlička, V., Změny vyvolané usídlením corynebacterium diphtriae na endokardu srdečnim ("endocarditis diphterica"), Časop. lék. česk. **75**:402, 440, 494, 510, 1936.
9. Buddingh, G. J., and Anderson, K., Acute vegetative endocarditis caused by bacillus diphtheriae, Arch. Int. Med. **59**:596, 1937.
10. Lenti, P., and Wirz, S., Étude clinique anatomo-pathologique et bacteriologique d'une septicémie à bacilles diphtériques avec endocardite, apparue au cours d'une angine diphtérique, Ann. méd. **44**:293, 1938.
11. Kaschel, H., Beitrag zur diphtheriebacillensepsis, Ztschr. f. Kinderh. **59**:437, 1938.
12. Wallner, E., Pseudodiphtheria okozta endocarditis septica, Orvosi hetil. **83**:716, 1939.
13. Galambos, J., Durch diphtheriebazillen verursachte endokarditis und sepsis, Deutsche med. Wchnschr. **67**:901, 1941.
14. Pull, E., Een geval van sepsis en endocarditis veroorzaakt door corynebacterium diphtheriae, Maandschr. v. kindergeneesk. **14**:93, 1946.
15. Skinner, J. W., Pencillin in persistent diphtheria, U. S. Nav. M. Bull. **45**:264, 1945.
16. Karelitz, S., and others, Penicillin in treatment of diphtheria and diphtheria carriers, J. Pediat. **30**:18, 1947.
17. Hewitt, L. F., Protection by streptomycin, penicillin and licheniformin against C. diphtheriae infections, Brit. J. Exper. Path. **29**:289, 1938.
18. Lankford, C. E., and Lacy, H., In vitro response of staphylococcus to aureomycin, streptomycin and penicillin, Texas Rep. Biol. & Med. **7**:111, 1949.

SPANISH ABSTRACT

Tratamiento Satisfactorio de la Endocarditis Bactérica Subaguda debida a C. Difteria con Penicilina y Estreptomicina.

La C. Difteria es un organismo causante raro en la endocarditis bactérica subaguda pues solamente 17 casos han sido registrados y ninguno de éstos ha vivido. La niñita da 8 años en este informe es el primer paciente que se alivió. Esta niña tuvo dos cultivos de sangre positivos para cepa de C. difteria virulenta intermedia, la que fué sensitiva a 0.05 u./ml. de penicilina y a 3.0 u./ml. de estreptomicina. El paciente recibió terapia de penicilina por un mes y respondió muy poco. Hubo una mejoría dramatica cuando se le administró también la estreptomicina. Este experimento clínico tiende a substanciar el trabajo de Hewitt en animales, el que demuestra que la estreptomicina es mucho más eficaz que la penicilina en salvar los cobayos inyectados con C. difteria. En ensayos *in vitro* con el organismo aislado en este paciente no revelaron ni prueba de sinergismo ni antagonismo cuando estudiados con combinaciones de penicilina, estreptomicina, sulfadiazina de sodio y aureomicina. Se sugiera para casos futuros que se use una combinación de penicilina y estreptomicina y que se hagan análisis de sensitividad en el organismo de manera que el médico pueda determinar la propia dosis de antibiotíco.

University of Texas School of Medicine

QUANTITATIVE METHOD FOR MEASURING H. PERTUSSIS ANTIBODY

By HATTIE E. ALEXANDER, M.D., CATHERINE MACPHERSON, PH.D., AND WINIFRED REDMAN, A.B.
New York City

DURING the organization of a large scale investigation of the value of therapeutic agents for the treatment of pertussis, it became apparent that a better method is needed for measuring antibody in therapeutic antisera in order to standardize the schedule and dosage. There is ample evidence from experience with treatment of pneumococcal[1] and H. influenzae infections[2] that a quantitative approach is necessary for the evaluation of serum therapy. To attain this end two requirements have been investigated: a quantitative method for measuring the curative antibody in therapeutic antisera and an objective basis for assessing the adequacy of a given dose for an individual patient. The results will form the basis of this report.

MATERIALS AND METHODS

Agglutinin Nitrogen Content of Therapeutic Antisera—The procedure used for the quantitative measurement of H. pertussis antibody is a modification of the method used originally by Heidelberger and Kabat for determining agglutinin nitrogen in rabbit antipneumococcal sera[3,4] and subsequently in collaboration with us in H. influenzae antiserum.[5]

The method depends upon the addition of an accurately measured amount of a washed bacterial suspension to an accurately measured volume of antiserum, the relative amounts being so chosen, if possible, that the bacteria are in excess. After agglutination is complete, the difference between the nitrogen content of the agglutinated bacilli, suitably washed, and that of the same quantity of unagglutinated bacilli gives the agglutinin nitrogen removed during each absorption from the volume of serum chosen. The supernatant is tested to make certain that all antibody has been removed; if not, adsorption on bacteria is repeated until this point is reached. The details of the method will be published elsewhere.

Bacterial Suspensions—A single phase I strain of H. pertussis #18323* was used for all bacterial suspensions employed in measuring agglutinin nitrogen. For slide agglutination tests vaccines were made from 2 strains of phase I H. pertussis #18323 and #10526.* Starting with a culture preserved and sealed under vacuum[6] the desiccated organisms were suspended in nutrient broth by adding 0.2 ml. to the tube in which the culture was dried, and this suspension used to seed the surface of a Bordet-Gengou agar (Difco) plate. After 48 hrs. incubation, the growth was transferred to broth 1 ml. and seeded in 0.5 ml. quantities on each of 2 Bordet-Gengou agar plates; the growth following incubation for 24 hrs. was suspended in broth 5 ml.; 0.5 ml. quantities were seeded on each of 10 Bordet-Gengou agar plates. The growth after 24 hrs. was removed from each of these plates with 5 ml. of neopeptone broth. The suspensions from the 10 plates were combined and 0.5 ml. quantities were seeded on each of 100 plates of Bordet-Gengou agar. The 24 hr.

From the Babies Hospital and the Department of Pediatrics, Columbia University College of Physicians and Surgeons, New York, N.Y.

The work reported in this communication was supported by grants from The Commonwealth Fund and The National Institutes of Health.

Presented before the 59th Annual Meeting of the American Pediatric Society, Atlantic City, N.J., May 5, 1949.

(Received for publication June 22, 1949.)

* Supplied by Dr. Pearl Kendrick.

growth was used for analyzing the antisera after the following preparation. To each plate was added 5 ml. 0.2% formalin in saline and the growth was removed by gently scraping the surface with a smooth-tip pipette. The total yield from the 100 plates was centrifuged in the cold, the supernatant decanted, and the cells were washed twice in 0.2% formalin in saline. All centrifuging was carried out in a refrigerated centrifuge at 0° to 4° C. When used for slide agglutination test this suspension in formalinized saline is centrifuged at low speed (1000 RPM) for 3 min. and adjusted to a turbidity corresponding to 3 billion organisms/ml.; after storage at 0° to 5° C. for 3 mos. no sign of deterioration could be detected. When used for measuring agglutinin nitrogen this suspension was washed twice in the cold with chilled saline to remove the formalin and any remaining constituents of the culture medium and adjusted to such a final volume that 1 ml. contains 0.5 to 1.0 mg. of bacterial nitrogen.

EXPERIMENTAL

Two human and two rabbit H. pertussis antisera have been examined for their content of agglutinin nitrogen. Human serum #1, supplied by Cutter Laboratories, is the gamma globulin fraction of 25 ml. of serum from immunized donors, dissolved in saline 2.5 ml. Human serum #2, produced by the Philadelphia Serum Exchange, is a lyophilized product reconstituted to half of its original volume, each vial containing the solids from 20 ml. of serum diluted in saline 10 ml. The two samples of rabbit serum, supplied by the New York State Department of Health, had been concentrated approximately six and eight times, respectively, and were furnished in vials containing 10 ml. each.

The results are shown in Table I. The right-hand column under Absorption 1 gives the agglutinin nitrogen recovered from each sample on the first run. In the column designated Absorptions 2-5, the figure for each serum represents the sum of subsequent recoveries following the initial absorption. In the next-to-last column is shown the

TABLE I

AGGLUTININ NITROGEN CARRIED DOWN FROM ANTIPERTUSSIS SERA BY H. PERTUSSIS SUSPENSIONS

Sera	Dilution	Absorption 1			Absorptions 2–5		
		N Content of Control Suspension	N Content of Agglutinated suspension #1	Difference Agglutinin N	Sum of Agglutinin N	Total Agglutinin N/ml. Whole Concentrate	Agglutinin N/ml. Original Serum
		mg.	mg.	mg.	mg.	mg.	mg.
Human							
1	2:5	1.14	1.23	0.09	0.045	0.34	0.034
2	2:5	1.14	1.16	0.02	0.025	0.11	0.055
Rabbit							
1	1:5	1.14	1.37	0.23	0.145	1.88	0.31
2*	1:1	1.08	1.43	0.35	0.61	1.92	0.24
2†	1:1	0.82	1.30	0.48	0.67	2.30	0.29

Human #1 and 2—4 absorptions removed agglutinins
Rabbit #1 —4 absorptions failed to remove all agglutinins
Rabbit #2* —5 absorptions failed to remove all agglutinins.
Rabbit #2† —2 of the 5 absorptions incubated at 37° C. 3 hr.

antibody content per ml. of each therapeutic agent as it is distributed; in the final column, the antibody concentration in the original serum, prior to processing, has been calculated. With regard to the two preparations of human serum, it is evident that their antibody content per vial representing 2.5 ml. and 10 ml., respectively, is not significantly different —0.85 mg. for #1 and 1.1 mg. for #2.

Both rabbit antisera analyzed contained a much higher concentration of antibody than either of the human antisera, even though the values measured do not even represent the total antibody in the sera; serum #1 was incompletely cleared after four absorptions, and #2 still showed an agglutinin titer of 1:12000 after five absorptions. It is apparent that the rabbit produces a much higher concentration of antibody than man as judged by agglutinin nitrogen content as well as by titer. Each 10 ml. vial of the rabbit therapeutic sera analyzed contains approximately 20 mg. of agglutinin nitrogen, in contrast to approximately 1 mg. per vial of human antiserum.

In pneumococcal and H. influenzae antisera, in which the protective antibody is anticarbohydrate, virtually all of the antibody is removed from the antiserum during the first absorption. The situation differs greatly with H. pertussis rabbit antibody; while the first absorption removes a larger quantity than any subsequent one, a number of absorptions—4 to 7, depending upon the temperature and other factors—are required to remove all the antibody. Investigations are being carried out to determine the most efficient method. The figures in the last line of Table I were obtained when two of the absorptions of rabbit antiserum #2 were carried out at 37° C. for three hours instead of 0° C. for 24 hours as were all other absorptions; they suggest that determination of agglutinin nitrogen in H. pertussis rabbit antiserum can be measured more efficiently when the reaction between antigen and antibody takes place at 37° C. than at 0° C.[3,4]

To study the specificity of measured agglutinin nitrogen for H. pertussis, a pool of sera from 30 infants aged 3 to 6 months, prior to any immunization, was examined for its agglutinin content; the H. pertussis suspensions failed to remove a measurable amount of nitrogen from the serum. Ordinary slide and tube agglutinin tests likewise failed to show any pertussis antibody in the pooled serum.

Adequacy of a Given Dosage for an Individual Patient.—For study of the adequacy of a given dose for an individual patient a simple rapid test has been investigated as an index of absence or presence of free antibody and the degree of excess in the sera of patients after antiserum administration. The procedure is carried out on a large glass slide (5 x 7 in.) divided into circles one inch in diameter by a glass-marking crayon. A heavy suspension of H. pertussis (250 by the Klett-Summerson photoelectric colorimeter, approximately 3 billion organisms per ml.) in 0.2% formalinized saline is added in 0.1 ml. quantity to an equal amount of each of the dilutions of patient's serum (two-fold from 1:2 through 1:64 for those treated with human serum and through 1:4000 for those receiving rabbit antiserum). The slide is rotated by hand for three minutes to mix thoroughly the vaccine with the antiserum and a reading is recorded after standing for one hour at room temperature. When the serum contains a high concentration of antibody, agglutination takes place immediately; when there are only small amounts more time is necessary for the reaction to take place.

To date about 15 children have been treated for pertussis with human hyperimmune serum #1 (the gamma globulin fraction) and an equal number with rabbit antiserum. All of the patients who received human antiserum were injected intramuscularly with a single dose of four vials (10 ml.). Rabbit serum was also administered intramuscularly

in one dose, according to the following schedule: under 3 mo., 15 ml.; 3 mo. to one yr., 20 ml.; 1 to 3 yr., 30 ml. Before injection of the therapeutic antisera the sera of all patients in both groups failed to agglutinate H. pertussis. The total dose of human antibody given to each patient contained 3.4 mg. of agglutinin nitrogen, and the total agglutinin nitrogen in the rabbit antiserum administered was approximately 30 to 60 mg. depending upon the age. The degree of antibody excess present in the sera of 10 patients treated with human antiserum and 10 with rabbit antibody two and seven days after serum administration is shown by the relative agglutinin titers listed in Table II. It is apparent that in patients with pertussis the larger the quantity of agglutinin nitrogen

TABLE II

TITER OF AGGLUTININS IN SERA OF PATIENTS RECEIVING EITHER HUMAN ANTIBODY (3.4 MG.) OR RABBIT ANTIBODY (30 to 60 MG.)

Patients	Human Antibody			Rabbit Antibody		
	Age (mo.)	Days After Serum 2	7	Age (mo.)	Days After Serum 2	7
1	2	1:32	1:16	2	1:1000	1:2000
2	1	1:8	1:8	8	1:2000	1:2000
3	5	—	1:64	10	1:1000	1:2000
4	3	1:128	1:64	2	1:2000	1:2000
5	4	1:64	1:32	19	1:4000	1:4000
6	36	1:8	1:8	5	1:2000	1:2000
7	2½	1:16	1:64	2	1:2000	1:4000
8	10	1:8	1:16	4	1:1000	1:2000
9	3	1:32	1:32	8	1:1000	1:1000
10	4	1:32	1:32	3½	1:8000	1:2000

administered, the higher the relative agglutinin titer in the circulating blood. The age ranges of the two groups are comparable; therefore the greater concentration of excess antibody after rabbit serum is not due to a smaller dilution factor. These data are of value at present only in confirming what quantitative agglutinin studies and mouse protection tests already indicate, that the rabbit produces a higher concentration of H. pertussis antibody than man. The degree of excess of antibody necessary for optimal results in serum therapy is under investigation.

DISCUSSION

The data presented suggest that the quantitative agglutinin nitrogen method is applicable to H. pertussis human and rabbit antiserum for measurement of H. pertussis antibody. The use of this procedure as a guide to size of the therapeutic dose must await proof that agglutinin nitrogen content is a measure of the curative substance in the antiserum. The results of preliminary experiments carried out in collaboration with Dr. Pearl Kendrick suggest that reduction of agglutinin nitrogen content as the result of absorption with suspensions of H. pertussis is accompanied by a reduction in mouse protective power. These investigations will be published in a separate report.

It is apparent that the optimal therapeutic dose of H. pertussis antibody has not been determined and that standards recommended previously—one vial every other day until the patient shows improvement—are unsatisfactory. There is reason to believe from

our experience with other forms of serum therapy that administration at one time of the total dose needed results in more efficient utilization of antibody. It may be only a coincidence that the vials of each of the two human antisera available contain approximately the same amount of antibody. On the other hand, it is not surprising since approximately the same volume of a pool of serum obtained from a number of similarly immunized adults has been processed.

The different rabbit therapeutic antisera analyzed showed a much greater concentration of antibody than the two human antisera. Whether this difference in immune response is the result of the intravenous route of vaccine administration in the rabbit as opposed to the subcutaneous route in the human or whether the rabbit is a more efficient antibody producer than man has not been determined.

Summary

A quantitative chemical method which determines the agglutinin nitrogen content has been shown to be applicable to H. pertussis therapeutic antisera.

The two human H. pertussis antisera available for therapeutic purposes contain approximately the same agglutinin nitrogen content per vial, about 1 mg. A vial of the two rabbit antisera analyzed contains approximately 20 mg. of agglutinin nitrogen.

A simple slide agglutination test is offered as a procedure for determining the degree of antibody excess in the sera of patients after serum therapy. The greater the content of agglutinin nitrogen in the therapeutic antiserum administered, the higher the relative agglutinin titer in the patient's serum.

References

1. Horsfall, F. L., Jr., Goodner, K., MacLeod, C. M., and Harris, A. H., Antipneumococcus rabbit serum as therapeutic agent in lobar pneumonia, J.A.M.A. **108**:1483, 1937.
2. Alexander, Hattie E., Treatment of haemophilus influenzae infections and of meningococcic and pneumococcic meningitis, Am. J. Dis. Child. **66**:172, 1943.
3. Heidelberger, M., and Kabat, E. A., Chemical studies on bacterial agglutination: Method, J. Exper. Med. **60**:643, 1934.
4 Heidelberger, M., and Kabat, E. A., Chemical studies on bacterial agglutination: Quantitative data on pneumococcus R (Dawson S) anti-R (S) systems, J. Exper. Med. **67**:545, 1938.
5. Alexander, Hattie E., and Heidelberger, M., Chemical studies on bacterial agglutination. V. Agglutinin and precipitin content of antisera to Haemophilus influenzae, type b, J. Exper. Med. **71**:1, 1940.
6. Brown, J. H., Vacuum tubes for storage and shipment of bacteria, Science **44**:429, 1926.

Spanish Abstract

Método Cuantitativo para Medir Anticuerpo H. Pertussis

Se ha demostrado que un método químico cuantitativo que determina el contenido nitrogeno aglutinina es aplicable a los antisueros terapeuticos de tos ferina.

Los dos antisueros de tos ferina humana obtenibles para objetos terapeuticos contienen aproximadamente el mismo contenido de nitrogeno aglutinina por frasco, cerca de 1 mg. Un frasco de dos anticuerpos de conejo analizado contiene aproximadamente 20 mg. de nitrogeno aglutinina.

Un simple análisis de aglutinación en lámina de vidrio se ofrece como un procedimiento para determinar el grado de exceso de anticuerpo en los sueros de pacientes después de la terapia de suero. Entre más grande es el contenido de nitrogeno aglutinina en el antisuero terapeutico administrado, más alto es el título de aglutinina relativo en el suero del paciente.

622 West 168th Street

GEMONAL® (5,5-DIETHYL 1-METHYL BARBITURIC ACID)

New Drug for Convulsive and Related Disorders

By M. A. PERLSTEIN, M.D.
Chicago

MANY new drugs have appeared recently for the treatment of epilepsy and related convulsive disorders. Since no one drug is effective in all types of epilepsy, it often becomes necessary to change medication or to use combinations of drugs in individual cases. Thus any new drug which offers promise of therapeutic value in epilepsy should be a welcome addition to the physicians' therapeutic armamentarium.

Of the existing barbiturates, those most commonly employed in epilepsy are phenobarbital and N-methyl-5-phenyl-5-ethyl barbituric acid (mebaral®). Most other barbiturates have a hypnotic or soporific effect out of proportion to their anticonvulsant action. Recently a new drug, gemonal®,* has been advocated by Everett and Richards[1] as a possible anticonvulsant. This report deals with a preliminary experience with this drug in 50 cases of epilepsy.

Gemonal® is chemically 5,5-diethyl 1-methyl barbituric acid. It is a white powder slightly soluble in water and is unstable in alkaline solutions. It has been shown to possess remarkable anticonvulsant activity against pentamethylenetetrazole (metrazol®) in mice and cats in doses which produce no sedation.[1]

The lethal dose in these animals was approximately 250 mg./kg. body weight. In doses of 50 mg./kg. orally gemonal® was highly protective against fatal convulsive doses of metrazol® in mice. In comparative tests, phenobarbital was found to afford similar anticonvulsant protection in the same dosage but caused greater sedation.

Gemonal® was supplied to the author for clinical use in a 0.1 gm. scored tablet. It was given to 50 patients with convulsive or related disorders. They varied in ages from 4 months to 64 years, the average age being about 8 years. There were 30 males and 20 females; 13 were Negroes, and the remainder white.

Table I gives the details of the observations on these 50 cases. The dosages of gemonal® varied from .02 to .18 gm. given one to four times daily for periods ranging from one week to three years. The dose prescribed usually was 1½ to 2 times that of phenobarbital. Improvement was considered as being present if the effect of the drug was dramatic and unquestionable in lessening the number and severity of spells by at least 33⅓%. Questionable or minor improvement was not counted in this category. In five instances where improvement was noted there were relapses when the drug was inadvertently stopped. Results are summarized according to diagnosis in Table II.

As will be noted in a total of 58 instances, benefit was noted in 21 and no benefit in 37. Of 32 cases with grand mal, nine were helped; of 14 cases with petit mal, four were improved; in 11 cases with myoclonic spells, eight were benefited; in the one

---

From Children's Neurology Clinic of the Cook County Hospital, Chicago, Ill.
(Received for publication June 6, 1949.)

* Produced by Abbott Laboratories and supplied by Dr. Richard K. Richards, Department of Pharmacology, Abbott Laboratories, North Chicago, Ill.

TABLE I

Case	Age	Sex	Race	Diagnosis and Type of Seizure	Dosage (gm.)	Length of Time on Drug	Result	Complications
RC	4 mo.	M	W	Jacksonian with Rigidity—OBD	.02 tid	Start 5/2/49	Marked benefit	
RM	7 mo.	F	N	GM—Post Enceph.	.02 tid	7 mo.	Marked benefit	
JW	10 mo.	M	W	PM with GM Jacksonian—OBD	.04 tid	3 wk.	Marked benefit	
LS	10 mo.	M	W	Myoclonus—OBD	.04 tid	5 mo.	No benefit	
RJ	1 yr.	M	W	GM—OBD	.02 tid	1 mo.	No benefit	
NR	1 yr.	M	N	GM—Idio	.04 tid	1 mo.	No benefit	Less soporific than phenobarb.
DP	16 mo.	F	W	Myoclonus—OBD	.04 tid	1 mo.	50% improvement	
LA	1½ yr.	F	W	Myoclonus—OBD	.04 tid	2 wk.	Marked benefit	
NW	1½ yr.	F	W	PM—OBD	.04 tid	2 wk.	Marked benefit	
SL	1½ yr.	M	W	GM—Myoclonus—OBD	.04 tid	3 wk.	No benefit	
DJ	20 mo.	M	W	GM—Myoclonus OBD	.04 tid	6 mo.	Marked benefit	No recurrence after stopping Rx
HH	20 mo.	M	W	GM—Idio	.09 bid	1 wk.	No benefit	
BN	3 yr.	F	W	PM and Akinetic—OBD	.02 tid	5 mo.	Marked benefit	
GG	3 yr.	M	W	GM—Myoclonus—OBD	.04 tid	2 mo.	GM—no benefit Myoclonus—improved	
RP	3 yr.	M	W	Myoclonus—OBD	.04 qid	4 mo.	Marked benefit	
NC	3½ yr.	F	W	GM—OBD	.09 tid	3 wk.	No benefit	
DK	4 yr.	F	W	GM—OBD	.04 tid	3 wk.	No benefit	
DS	4 yr.	M	W	Myoclonus–Tuberous Sclerosis	.04 tid	1 mo.	No benefit	
JP	4 yr.	F	W	PM—Idio	.04 qid	2 mo.	No benefit	Sleepy
SW	4 yr.	F	W	PM—OBD	.02 tid	1 wk.	Worse	
RP	5 yr	M	W	Psychomotor—OBD	.04 tid	2 wk.	No benefit	
WH	5 yr.	M	W	Myoclonus—OBD	.04 tid	5 mo.	Marked benefit	
RH	5 yr.	F	W	GM—OBD	.09 once daily	1 wk.	Worse	
DL	5 yr.	M	W	GM—Myoclonus—OBD	.04 bid	9 mo.	50% improvement	
RB	6½ yr.	M	W	PM—Idio	.04 bid & tid	3 wk. 4 wk.	No benefit	
RL	7 yr.	M	W	GM—Idio	.09 tid	2 mo.	No benefit	
JH	7½ yr.	F	W	PM—GM—OBD	.04 qid .09 qid	1 wk. 3 yr.	PM—marked benefit GM—no benefit	
MA	8 yr.	F	W	PM, GM—Idio	.18 gm. once daily	1 wk.	No benefit	Morbilliform rash
WB	8 yr.	M	W	PM—Idio	.04 tid	3 wk.	Worse	
MS	8 yr.	M	N	Akinetic—OBD Post Traumatic	.09 tid	2 wk.	No benefit	
TT	8½ yr.	M	W	PM—Idio	.04 bid	1 wk.	No benefit	
HP	9 yr.	M	N	GM Jacksonian Post Enceph.	.06 tid .09	4 mo.	Marked benefit	
CG	9 yr.	M	W	PM—Idio	.09 tid	2 wk.	Worse	
AE	9½ yr.	M	N	GM—Idio	.09 tid	2 wk.	No benefit	
LD	10 yr.	M	N	GM—OBD	.09 tid	3 mo.	Moderate benefit; better than phenobarb.	
EL	10 yr.	F	N	GM—Idio	.09 daily	3 mo.	No benefit	
RS	10 yr.	M	N	GM—OBD	.09 tid	2 mo.	No benefit	
MD	10 yr.	F	N	Jacksonian GM—OBD	.09 qid	3 mo.	Moderate benefit	
TD	10 yr.	F	N	PM—Idio	.09 tid	1 mo.	Slight benefit	
RD	11 yr.	M	N	Jacksonian GM—OBD	.09 tid	1 wk.	No benefit	
MW	12 yr.	F	W	GM—Rt Spastic Hemiplegia	.09 tid	1 mo.	Marked benefit	
EB	12 yr.	M	W	GM—PM—Idio	.06 tid	3 mo.	No benefit	
PK	12 yr.	F	W	PM—Idio	.04 tid	7 wk.	Marked benefit	
DJ	15 yr.	F	W	GM—Akinetic—OBD	.09 bid	3 wk.	No benefit	
GM	15 yr.	M	N	GM—Post Enceph.	.09 tid	1 mo.	No benefit	
CT	17 yr.	M	N	GM—Idio	.09 bid	1 wk.	No benefit	
LM	17½ yr.	F	W	PM—OBD	.09 tid	6 wk.	No benefit	
FP	18 yr.	F	W	GM—OBD	.09 qid	3 wk.	No benefit	
BC	32 yr.	M	W	GM—Idio	.09 bid	8 wk.	No benefit	
MW	64 yr.	M	W	GM—Arteriosclerosis	.09 bid	5 mo.	Marked benefit	

GM—Grand Mal; PM—Petit Mal; OBD—Organic brain disease.

TABLE II

Diagnosis	Total Cases	Results	
		Improved	Not Improved
Grand Mal—Total	32	9	23
Idiopathic	9*	0	9
Organic	23†	9	14
Petit Mal—Total	14	4	10
Idiopathic	9	1	8
Organic	5	3	2
Myoclonic (Organic)	11	8	3
Psychomotor (Organic)	1	0	1
Total	58	21	37

* Two also had Petit Mal.
† Two also had Petit Mal, 4, also myoclonus.
(This explains the total of 58 observations on 50 cases.)

remaining case of psychomotor epilepsy, there was no benefit. Although the number of cases is too small from which to draw definite conclusions, it is noteworthy that gemonal® was most effective in the myoclonic forms of epilepsy, a condition especially resistant to other anticonvulsant drugs. Most of the patients with myoclonic spells had previously been tried on other forms of medication without success.

When the cases are dichotomized as in Table III into those with idiopathic epilepsy and those due to organic brain disease it is seen that of 35 cases of epilepsy associated

TABLE III

Diagnosis	Total Cases	Results	
		Improved	Not Improved
Organic	35	18	17
Idiopathic	15	1	14
Total	50	19	31

with organic brain disease, there was improvement in 18 instances. In only one of the 15 cases of idiopathic epilepsy was improvement noted.

If these observations should be corroborated by further study, gemonal® would be a most valuable drug for epilepsy, since its greater effectiveness in the organic than in the idiopathic form of disease would make it unique among the antiepileptic drugs.

Gemonal®, like mebaral®, appears to have less soporific effect than phenobarbital. It is relatively nontoxic. Only one morbilliform rash was observed. No blood changes were noted in any case in the three years it has been used. It is valuable as an adjuvant or alternate drug where other drugs may fail to control seizures.

Conclusions

Gemonal®, a relatively new, nontoxic, anticonvulsant barbiturate was employed in 50 cases of epilepsy. In this series it was of practically no benefit in idiopathic epilepsy, but improved 18 of 35 cases with seizures due to organic brain disease. Noteworthy was the rather consistent improvement in patients with myoclonic attacks.

Reference

1. Everett, G. M., and Richards, R. K., Anticonvulsant action of drugs against Metrazol and antiepileptic activity, Fed. Proc. 5:26, 1946.

Spanish Abstract

Gemonal® (5,5-Dietilo 1-Metilo Acido Barbitúrico); Nueva Droga para Trastornos Convulsivos y Relacionados

El Gemonal® (5,5-dietilo 1-metilo ácido barbitúrico) es un nuevo barbitúrico anticonvulsivo que no es tóxico. Se encontró que en una serie de 50 casos de epilepsia no fué de casi ningún provecho en formas idiopáticas de la enfermedad; pero 18 a 35 casos mejoraron definitivamente con ataques debidos a enfermedad orgánica del cerebro.

Esta propiedad de ser más eficaz en epilepsia más bien orgánica queidiopática es única entre las drogas antiepilepticas. Se notaron mayores beneficios de la droga en casos caracterizados por ataques mioclónicos.

4743 North Drake Avenue

TREATMENT OF HEMOPHILUS INFLUENZAE b MENINGITIS

Report of 67 Cases

By KATHRYN J. MCMORROW, M.D., M.P.H., AND FRANKLIN H. TOP, M.D., M.P.H., F.A.C.P.
Detroit

THE treatment of meningitis caused by H. influenzae b has changed rapidly since Fothergill's report[1] in 1937. He reported 201 cases with a fatality rate of 84.6%. About that time the first chemotherapeutic agents were being introduced, and Lindsay[2] treated a series of 108 cases with sulfonamide derivatives and had a fatality rate of 54%. At approximately the same time Alexander[3] reported on the experimental use of anti-influenzal rabbit serum. Later the use of this agent on human cases reduced the fatality rate to approximately 20% as reported by Alexander[4] and others.[5-8]

TABLE I

DISTRIBUTION OF CASES AND DEATHS BY AGE GROUP

Age Group	Cases	Deaths	Fatality Rate %
Under 2 yr.	33	11	33.3
2– 4 yr.	19	2	10.5
5– 9 yr.	6	1	(16.7)
10–14 yr.	3	0	—
15+ yr.	6	3	(50.0)
Totals	67	17	25.4

Streptomycin is one of the new antibiotic agents to be used in the treatment of influenzal meningitis. Experimental work was reported by Alexander[9] in 1946, and she later indicated that streptomycin was of definite value clinically.[10] More recently Alexander[11] summarized her experience and laid down the general principles of therapy of H. influenzae meningitis, with particular reference to the role of antibiotics.

The present report extends from January 1943 through September 1948, covering an experience in the treatment of H. influenzae b meningitis at the Herman Kiefer Hospital in Detroit.

The series comprises 67 consecutive cases: 38 male and 29 female. Table I shows the age distribution of cases and the influence of this factor on mortality. Nearly one half, or 33 cases, were under 2 years of age. The group under 2 years of age accounted for 50% of the cases and 65% of the deaths. The fatality rate for this group was 33.3%. The number of patients by age groups above 5 years was too small to provide reliable rates.

The median day of disease on which treatment was begun falls for the entire group of 67 patients on the fourth day. For the group under 2 it falls on the fifth.

From the Detroit Department of Health, the Department of Preventive Medicine, Wayne University College of Medicine and the Herman Kiefer Hospital, Detroit, Mich.
(Received for publication June 27, 1949.)

TABLE II

EFFECT OF PROMPTNESS OF TREATMENT

Age Group	Day of Illness on Which Treatment Was Started:													
	1	2	3	4	5	6	7	8	9	10	11	14	21	23
Under 2 yr.	ooo ox	oox	ooo ox	oo	ox	o	oox	—	o	o	o	ooo xx	xx	xx
2– 4 yr.	ox	ooo o	ooo oox	o		o	ooo	—	o					
5–9 yr.	o		o	ox	oo									
10–14 yr.			o	o	o									
15+ yr.			o	oox	x				x					

Legend: o = Recovered Case; x = Death

Table II illustrates the effect of promptness of the treatment. It suggests that delay in treatment in patients under 2 years of age has a definite bearing on the outcome. Three patients in every four recovered if treatment was begun within 14 days from onset; but if treatment were delayed until the end of the third week none of the patients in the age group under two recovered. When these four deaths are not considered, the fatality rate for the group becomes 24.1%. In the older age groups, six out of every seven cases treated on or before the seventh day recovered. Experience in the treatment of older patients where therapy was delayed beyond one week is too limited in this series for comment.

DIAGNOSIS

Diagnosis in all cases was confirmed by recovery of H. influenzae b on culture from the spinal fluid. Blood cultures were taken on each patient at the time of admission; 20 (30%) were positive for H. influenzae b. It is customary at the Herman Kiefer Hospital to give intravenous sulfadiazine to all patients in the admitting room as soon as the diagnosis of a purulent meningitis has been made; that is, directly following lumbar puncture and the taking of blood for culture. A concerted effort is made simultaneously to identify the causative organism on direct smear, making use of the quellung reaction wherever indicated. Additional immediate specific therapy is governed accordingly. Also, intramuscular penicillin is given in all cases where there is clinical evidence of a secondary meningitis following otitis media, sinusitis, pneumonia or sepsis.

In only a relatively small number of cases was H. influenzae b identified by direct smear. Hence, for the remainder, the administration of specific antiserum was delayed from 1 to 5 days awaiting blood or spinal fluid confirmation of H. influenzae b infection. During this time sulfonamides were being continued subcutaneously.

TREATMENT

Patients in this series may be grouped into five categories with relation to type of treatment given (see Table III).

The number of cases is too small in categories 2 (Sulfadiazine and streptomycin), 4 (Sulfadiazine only), and 5 (No specific therapy) for the fatality rate to be reliable. In this series the introduction of streptomycin had little apparent effect on outcome,

TABLE III

CASES AND DEATHS ACCORDING TO TYPE OF TREATMENT

Type of Treatment	Cases	Deaths	Fatality Rate %
1. Sulfadiazine and serum	37	6	16.2
2. Sulfadiazine and streptomycin	5	2	(40.0)
3. Sulfadiazine, serum and streptomycin	18	3	16.7
4. Sulfadiazine only	5	4	(80.0)
5. No specific therapy	2	2	(100.0)
Totals:	67	17	25.4

since the rates in categories 1 (Sulfadiazine and serum) and 3 (Sulfadiazine, serum, and streptomycin) are the same.

Table IV records the cases and deaths according to the type of treatment in the age group below 2 years. Only in category 1 (Sulfadiazine and serum) is the number of cases sufficient to make the fatality rate significant. In this category the fatality rate is reduced from 31.6% to 18.7% by disregarding the three deaths in which serotherapy was started after the 14th day. This corrected rate is similar to the fatality rate for the entire group treated with serum (16.2%). The fatality rates in category 3 (Sulfadiazine,

TABLE IV

CASES AND DEATHS ACCORDING TO TYPE OF TREATMENT IN AGE GROUP BELOW 2 YEARS

Type of Treatment	Cases	Deaths	Fatality Rate %
1. Sulfadiazine and serum	19	6	31.6
2. Sulfadiazine and streptomycin	0	0	—
3. Sulfadiazine, serum and streptomycin	10	2	20.0
4. Sulfadiazine only	3	2	(66.7)
5. No specific therapy	1	1	(100.0)
Totals	33	11	33.3

serum, and streptomycin) are similar in the group below 2 years of age (20.0%) and in the over-all group (16.7% in Table III).

Of those patients under 2 years of age who received serum during the second week of illness, 4 out of 5 recovered. However, only 3 of 8 recovered when serotherapy was delayed beyond the second week from onset. (See Table V).

Meningitis is notoriously difficult to diagnose in infants because the classical signs may be absent. That diagnostic acumen and judicious treatment could further reduce the fatality of H. influenzae b meningitis is evident from data in Table V, which relates to day of disease serum is first administered, and further the earlier the patient is seen and correctly diagnosed the more likely it is that treatment will be successful.

At various times the antiserum used was limited in supply; therefore, where larger doses were indicated it was possible to give only amounts on hand, sometimes half the indicated dosage. The criteria for evaluation of the amount of antibody nitrogen to be

TABLE V

OUTCOME OF PATIENTS UNDER 2 YEARS OF AGE GIVEN SERUM ACCORDING TO DAY OF ILLNESS

	Day of Illness:														
	1	2	3	4	5	6	7	8	9	10	13	15	17	25	26
		o		o	o	oo	o	o	x	oo	o	oo x	xx o	x	x

Legend: o = Recovered Case; x = Death

given were: (1) clinical state of the patient; (2) spinal fluid sugar determination; (3) quellung reaction.

Present experience indicates that the intramuscular route for serotherapy is equivalent to intravenous injection. Of 37 patients who received serum, 22 received intramuscular serum and one died; of the 13 who received serum intravenously, 4 died. Two patients received serum by both routes, one recovered. Severity of illness was not the determinant

TABLE VI

RECOVERIES AND DEATHS BY AGE GROUP ACCORDING TO TYPE OF TREATMENT

Age Group	Category*	Recovery	Death	Total	Comment
Under 2 yr.	1	13	6**	19	Treatment began after 21st day
	2	0	0	—	
	3	8	2**	10	" " "
	4	1	2**	3	36 hr. deaths
	5	0	1	1	
2– 4 yr.	1	11	0	11	
	2	2	0	2	
	3	4	0	4	
	4	0	2**	2	36 hr. deaths
	5	0	0	—	
5– 9 yr.	1	4	0	4	
	2	0	1*	1	Anuria Sulfa 9th day (CSF neg. treatment)
	3	1	0	1	
	4	0	0	—	
	5	0	0	—	
10–14 yr.	1	2	0	2	
	2	0	0	—	
	3	1	0	1	
	4	0	0	—	
	5	0	0	—	
15+ yr.	1	1	0	1	
	2	1	0	1	
	3	1	1	2	
	4	0	1*	1	Diabetic acidosis, 36 hr. death
	5	0	1	1	

Each star indicates 1 death mentioned under comment. See Table IV for description of categories 1–5.

for the route chosen. The intrathecal route is not used in the Herman Kiefer Hospital.

Table VI provides an interesting commentary on the prognosis of H. influenzae meningitis relative to diagnosis and treatment. There were five deaths which occurred 36 hours after admission. Sulfadiazine was administered in four of these during the brief period of hospitalization. This indicates that the offending organism could not be identified by smear and quellung on admission and that effective therapeusis could not be instituted at once. Uncontrolled diabetes was present in the fifth. A toxic reaction to sulfadiazine accounted for a sixth death. Deaths occurred in all four cases in which treatment began on the 21st day or later.

Summary

The present series consists of 67 patients, 17 of whom died, giving a gross fatality rate of 25.4%. Nearly one half of the cases were under 2 years of age and accounted for 65% of the deaths. By disregarding patients who died within 36 hours of admission and patients first admitted to the hospital after 21 days, the corrected fatality rate for the group below 2 years is 18.2%.

Death occurred in the four patients admitted and first treated at the end of the third week of illness. Both deaths in the group under 2 years who received sulfadiazine, serum and streptomycin occurred in patients who had been ill three weeks before receiving treatment.

The prognosis is likely to be unfavorable in the age group under 2 years if treatment is delayed beyond the 14th day.

The fatality rate for patients who received sulfadiazine and serum was the same in this series as for patients who received streptomycin in addition.

Serotherapy proved ineffectual in the age group under 2 years when delayed beyond the 14th day of illness. With respect to prognosis, the intravenous route for administration of serum offers no advantage over the intramuscular route.

References

1. Fothergill, L. D., Hemophilus influenzae meningitis and its specific treatment, New England J. Med. **216**:587, 1937.
2. Lindsay, T. W., and others, Treatment of meningitis due to hemophilus influenzae, J. Pediat. **17**:220, 1940.
3. Alexander, Hattie E., Experimental basis for treatment of haemophilus influenzae infections, Am. J. Dis. Child. **66**:160, 1943.
4. Alexander, Hattie E., Type b anti-influenzal rabbit serum for therapeutic purposes, Proc. Soc. Exper. Biol. & Med. **40**:313, 1939.
5. Alexander, Hattie E., Treatment of type b hemophilus influenzae meningitis, J. Pediat. **25**:517, 1944.
6. Beck, K. H., and Janney, F. R., Alexander's rabbit serum in treatment of influenzal meningitis, Am. J. Dis. Child. **73**:317, 1947.
7. Edmonds, A., and Neter, E., Appraisal of treatment of hemophilus influenzae type b meningitis with specific rabbit serum and sulfonamides, J. Pediat. **28**:462, 1946.
8. Smith, M. H. D., Wilson, P. E., and Hodes, H. L., Treatment of influenzal meningitis, J.A.M.A. **130**:331, 1946.
9. Alexander, Hattie E., Influence of streptomycin on type b H. influenzae, Science **104**:101, 1946.
10. Alexander, Hattie E., Hemophilus influenzae meningitis treated with streptomycin, J.A.M.A. **132**:434, 1946.
11. Alexander, Hattie E., Treatment of H. influenzae meningitis, J. Michigan State M. Soc. **46**: 193, 1947.

SPANISH ABSTRACT

Tratamiento de Influenzae Hemophilus b Meningitis; Informe de 67 Casos

La presente serie consiste de 67 pacientes, 17 de los cuales murieron, dando una proporción de fatalidad bruta de 25.4%. Casi la mitad de los casos fueron de menos de 2 años de edad y formaron el 65% de las muertes. No tomando en cuenta los pacientes que murieron dentro de 36 horas de admisión y pacientes admitidos en el hospital después de 21 días, la proporción de fatalidad corregida para el grupo de menos de 2 años es 18.2%.

La muerte vino a 4 pacientes admitidos que fueron tratados primero al fin de la tercera semana de enfermedad. Ambas muertes en el grupo de menos de 2 años que recibieron sulfadiazina, suero y estreptomicina ocurrió en pacientes que habían estado enfermos 3 semanas antes de recibir tratamiento.

El prognóstico probablemente no será favorable en el grupo de edad de menos de 2 años si el tratamiento se dilata más de catorce días.

La proporción de fatalidad para pacientes que recibieron sulfadiazina y suero fué la misma en esta serie que para pacientes que recibieron estreptomicina en adición.

La Sueroterapia no dió resultado en el grupo de edad de menos de 2 años cuando se dilató más de catorce días de enfermedad. Con respecto al prognóstico, la ruta intravenos para la administración de suero no ofrece ventaja alguna sobre la ruta intramuscular.

1151 Taylor Street

STUDIES OF AN OUTBREAK OF POLIOMYELITIS IN IOWA

With Reference to Familial Incidence and the Presence of Virus in Immediate Extra-Human Environment

By HERBERT A. WENNER, M.D., AND VERNON L. BRANSON, M.D.
Kansas City, Kan.

DURING the summer of 1948, a widespread outbreak of poliomyelitis occurred in Iowa. The epidemic began during the month of May in western counties of the state. The disease was studied in two western counties in order to review some facts regarding the natural evolution of the epidemic.

First, information was sought in regard to the frequency of household outbreaks of poliomyelitis. Extant data[1,2] indicate that the virus causing poliomyelitis is distributed widely among members of certain households in which the disease appears. Second, a search was made for poliomyelitis virus at some extra-human sources in a rural area. A search was made for virus at extra-human sources because onset of poliomyelitis in respective members of certain households occurs almost simultaneously, suggesting exposure of members at a common source. A rural area was selected because there are some indications that explosive outbreaks in families may be more common in rural than in urban areas. Observations and experimental studies made in two western counties during the 1948 outbreak of poliomyelitis form the basis of the present report.

METHODS AND MATERIALS

Epidemic area.—Sharp focal outbreaks of poliomyelitis occurred during the month of May (1948) in Harrison (pop: 23,000) and Pottawattamie (pop: 67,000) Counties in western Iowa. At the end of the year, 98 (attack rate, 4.3/M.) and 84 (attack rate, 1.3/M.) cases were reported in these counties, respectively. In all, 1,241 cases were reported in Iowa.

Harrison and Pottawattamie Counties are located in western Iowa. They are bounded on the west by the Missouri River. The adjacent bottom lands are traversed by numerous drainage ditches and creeks (Chart 1). There are also many small ponds and back water areas. East of the river (5 to 8 miles), the terrain changes to a low-hilled rolling countryside.

These counties are predominantly rural. Farming is the chief vocation. Sanitation is generally poor in the smaller communities and in rural residences. Pit privies, cesspools and septic tanks are commonly present. Human excreta has access to creeks and drainage ditches. No city or town in Harrison County has a modern sewage system. Raw sewage from 5 towns in Harrison County empties into the Boyer River. The same type of sanitation prevails in Pottawattamie County. Council Bluffs (pop: 41,500) has a sewer system; raw sewage enters the Missouri River. Many homes in Council Bluffs have privies or cesspools.

The water supply on rural residences is from driven wells. The small towns, such as Mondamin, have municipal wells. Council Bluffs obtains its water from the Missouri River. A sanitary survey by Mr. M. O. Nelson found each of the municipal water sources in "satisfactory condition."

Seasonal factors.—The spring and summer months were exceedingly dry. During the month of May, there was 0.56 in. of precipitation, compared with a normal of 3.77 in. The river was not at flood stage during the spring. This is mentioned because during the winter months, poliomyelitis

From the Departments of Pediatrics and Bacteriology and the Hixon Memorial Laboratory, University of Kansas School of Medicine, Kansas City, Kan.

Aided by a grant from the National Foundation for Infantile Paralysis, Inc.
(Received for publication June 8, 1949.)

(5 cases were reported) occurred in Sioux City, north of Harrison County. Sioux City sewage emptied directly into the Missouri River. Although flies were seen in May, they were not prevalent in uncommon numbers; most households remarked on their absence.

Family observations.—During the summer and fall of 1948, households of all recognized cases were visited. Each family was interviewed by a district health nurse* assigned to gather data about circumstances in and beyond the household, at and preceding the time poliomyelitis appeared.

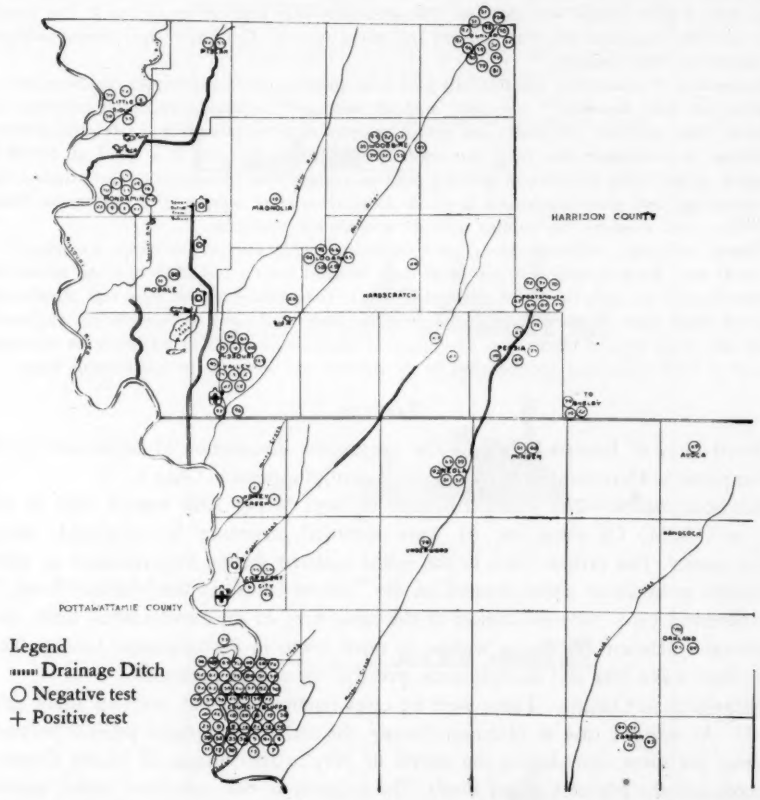


CHART 1. Outline map of Harrison and Pottawattamie Counties, Iowa. Each of numbered circles represents reported case of poliomyelitis. Waterways are indicated by name and linear markings. Symbols: water jugs = place of collection of sewage or water; outlines of birds, frogs or fish = sites where each was collected; + = positive test; 0 = negative test.

In the family interview, direct questions were asked about additional sick members in the household, the age, onset and type of illness in each. Households were visited within 1 wk. and again in 3 wks. following a reported case.

The method has limitations; obviously the more serious of them is lack of precise knowledge as to whether illness in familial associates was poliomyelitis or some other disease.

Human specimens.—Stool samples were obtained from 10 children. The patients had paralysis and

* The family histories were obtained largely by one individual. During May, the nurse, accompanied by the authors, visited on each of 3 days homes of reported patients. She participated in interviews. The data were recorded on a form used by the Iowa State Department of Health. Duplicate copies were forwarded to the authors for study.

were hospitalized. Stool samples were collected by hospital attendants and shipped to the Virus Laboratory packed in dry ice. On receipt, they were stored in a box containing dry ice until tested.

Extra-human specimens.—Birds were shot (May 28 to June 2) near open sewer conduits from villages or on the grounds of households where currently there was poliomyelitis. The species of birds included English sparrows, barn swallows, grackles, red-winged blackbirds and domestic pigeons. Three frogs were caught in shallow water in a pond adjacent to the household of 2 paralyzed children. Dead fish were obtained at Lynn Lake. Raw sewage and water from creeks potentially contaminated with human sewage was obtained. The specimens were kept on ice (12 hr.). The intestinal tracts of birds, frogs, and fish were removed and stored at −70° C. (4 to 6 days) during preparation for inoculation into monkeys.

Preparation of materials.—The methods used in preparation of stool specimens for inoculation into monkeys has been described.[3,4] The same methods were used in preparation of the intestinal tracts of birds, frogs and fish. The water and sewage samples were sedimented in a refrigerated Sharples centrifuge. A continuous flow rotor was used. The centrifuge was run at a speed of 40,000 rpm (roughly 50,000 times the force of gravity) with an average flow of one l./hr. The sediment lining the centrifuge bowl was resuspended in sterile distilled water to make a 20% suspension. Prior to inoculation into monkeys, the diluted material was treated with ether.

Animals.—Rhesus (*Macaca mulatta*) and cynomolgus (*Macaca irus*) monkeys, weighing 2 to 4 kg., were used. Each monkey was inoculated once intraperitoneally (10 to 20 cc.) and several times intranasally (3.0 cc. daily for 2 to 6 consecutive days). Temperature records were kept. Animals were observed twice daily. Monkeys were killed when symptoms and signs of poliomyelitis appeared, or at the end of 30 days of observation. Histologic examination of the CNS was made on all animals. Passage of CNS tissue was accomplished in the positive and some of the questionable tests.

Results

Distribution of Reported Cases.—The geographic distribution of recognized cases of poliomyelitis in Harrison and Pottawattamie Counties appears in Chart 1.

Harrison County.—The reported number of cases during 1948 was 98 with an attack rate of 4.3/M. Of these 98, 81 were recorded according to geographic location in the county. The earliest cases in the initial outburst during May occurred in western townships in or about towns situated on the "bottom lands" of the Missouri River. The first observed cases occurred almost at the same time in separated towns, Little Sioux, Mondamin, Missouri Valley, as well as in small towns in Pottawattamie County. Thereafter, there was a slow and discontinuous spread of the disease eastward.

Pottawattamie County.—There were 84 cases reported in 1948, with an attack rate of 1.3/M. As was the case in Harrison County, the earliest recognized patients became ill at about the same time during the month of May in the villages of Honey Creek and Crescent and the city of Council Bluffs. The majority of the cases were urban, inasmuch as they occurred in Council Bluffs. During the summer, there was a slow but not a remarkable spread of the disease to eastern townships.

Seasonal Distribution of Reported Cases.—The seasonal distribution of cases in Harrison and Pottawattamie Counties appears in Chart 2. Harrison and Pottawattamie Counties were involved more extensively than any of the neighboring counties.

Mention has been made of winter cases of poliomyelitis in Sioux City. It is noteworthy that early focal outbreaks of poliomyelitis, precursor to a later widespread prevalence in the state, occurred in Harrison and Pottawattamie Counties, south of Sioux City (Woodbury County) along the course of the Missouri River. At this time (May), the disease had not extended eastward.

Harrison County.—The discontinuous spread of the epidemic was evidenced by three separate peaks of incidence. The first "wave" occurred in May and early June, the second during July and the third and last wave during September. It seems clear that the dis-

continuous but advancing "waves" represented the implantation of virus within new communities east of the areas first involved. In a rural area, containing separated small towns, this kind of advance of an epidemic wave may not be unusual, but, in many ways, it has not been like the explosive and virtually simultaneous appearance of measles and influenza. At least the velocity of spread of the epidemic may be regarded as being dif-

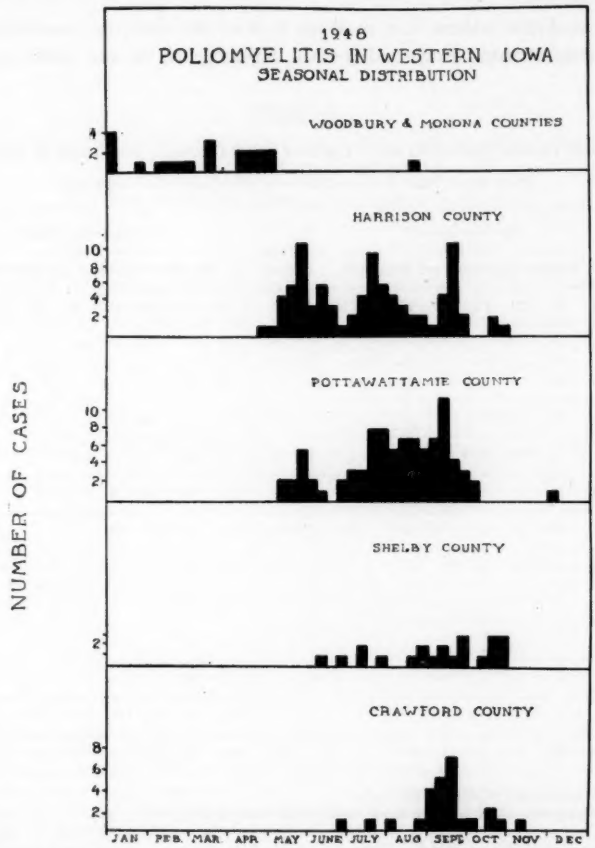


CHART 2. Seasonal distribution of reported cases of poliomyelitis in Harrison and Pottawattamie Counties, including comparative data for adjacent counties.

ferent from the latter, particularly in respect to the slow dispersal of poliomyelitic virus over a rather small geographic area.

Pottawattamie County.—The first recognized cases occurred in May, also. Following an initial outburst of 10 cases, particularly in small towns north of Council Bluffs, there was a brief period of apparent quiescence. Then, late in June, there was a substantial increase in the number of reported cases. In the main, the epidemic was an urban one. The epidemic in Council Bluffs did not attain velocity until July; the peak incidence was reached in September. During this period, there was extension of the disease to the smaller towns located in eastern townships.

Incidence of Illness in Households Attacked by Poliomyelitis.—Histories regarding illnesses were obtained on members in 145 households in Harrison and Pottawattamie Counties. Within these households, there was a reported incidence of 165 cases of poliomyelitis. The data in Tables I and II summarize these and additional illnesses* occurring among members in the respective households, when poliomyelitis attacks one or more of its members.

The data in Table I show that in about half of the observed households, regardless of size of membership, illness other than poliomyelitis in the index case† was not apparent.

TABLE I

INCIDENCE OF ILLNESS AMONG FAMILY MEMBERS OF HOUSEHOLDS ATTACKED BY POLIOMYELITIS

(Not more than 21 days before or after onset in index case)

No. Individuals per Household	Harrison County								Total Households	Pottawattomie County								Total Households
	No. Sick Individuals per Household									No. Sick Individuals per Household								
	I	II	III	IV	V	VI	VII	VIII		I	II	III	IV	V	VI	VII	VIII	
2	⑤	1							6	1								1
3	3	0							3	8	2							10
4	9	7	1	1					18	13	7	2						22
5	8	3	3	1					15	4	3	1						8
6	2	2	2	0	1				7	9	4	0	2					15
7	4	1	1	2	1	1			10	1	1	2	0					4
8	1	3	1	2	0	0	1		8	6	1		1					9
9			1	1	0	0	1		3	1	0			1				2
10										0	1						1	2
12										1	0							1
16										1	1							2
Total	32	17	9	7	2	1	2		70	45	20	5	3	1	0	0	1	75

Index case = 1st reported case of poliomyelitis.
⑤ = in 5 households each with 2 individuals, one member experienced illness.

In the remaining households, illness occurred in two or more members associated in the household with the index case. Data in Table II show that whenever poliomyelitis attacked one member (or more) in certain households, illness occurred in additional members almost at the same time as onset of the disease in the index case. In 16 (of 21) families in Harrison County, each consisting of five or more members, there were three, and often more, individuals with recognized illness occurring at a time close to onset of poliomyelitis (one to five days) in the index case. In Pottawattamie County, six

* The additional illnesses in other family members consisted of (1) paralytic poliomyelitis, (2) abortive poliomyelitis, characterized by fever, headache, stiff neck and muscle pains and (3) minor, poorly-defined complaints characterized by fever, headache, sore throat or, in the case of young children, an unusual behavior, namely fever, irritability or restlessness.

† The index case represents the first individual to have frank poliomyelitis, but not necessarily the first individual in the household who has acquired the disease.

(of 10) families, each containing four or more members, experienced illness in familial associates of the index case.

The data appearing as ratio at the base of Table II set apart those families in which many members of a household were attacked almost simultaneously, in comparison with families experiencing illness in several members three to six weeks apart from onset of poliomyelitis in the index case. For example, in Harrison County, in 10 (of 17) families, there were two members—and in six (of nine) families, there were three members, sick at virtually the same time. It is impossible to state that all of these illnesses were polio-

TABLE II

INCIDENCE OF 2 OR MORE ILLNESSES AMONG FAMILY MEMBERS OF HOUSEHOLDS ATTACKED BY POLIOMYELITIS

(Not more than 7 days before or after onset in index case)

No. Individuals per Household	Harrison County							Total	Pottawattamie County							Total
	No. Sick Individuals per Household								No. Sick Individuals per Household							
	II	III	IV	V	VI	VII	VIII		II	III	IV	V	VI	VII	VIII	
2	1							1	1							1
3	0								4							4
4	3							3	2	1						3
5	0	3						3	4	0	2					6
6	2	1						3	1	1	0					2
7	1	0	2	1	1			5	1		1					2
8	3	1	2	1		1		8	0			1				1
9		1	1			1		3	1							1
10									0						1	1
16									1							1
Total	10	6	5	2	1	2	—	26	15	2	3	1	—	—	1	22
Ratio*	10/17	6/9	5/7	2/2	1/1	2/2	—	26/70	15/20	2/5	3/3	1/1	—	—	1/1	22/75

* The ratio is obtained by taking the horizontal totals in Tables I and II and determining the comparative number of house holds in which illness was simultaneous with or apart from onset of poliomyelitis in the index case.

For legend, see Table I.

myelitis. In particular this is true of the families experiencing illnesses of minor nature several weeks preceding onset of poliomyelitis in the index case. The data indicate, however, that it is easier to delineate simultaneous illnesses occurring in large families composed of young members than in small ones with adults or older children representing the household at risk.

A number of these illnesses clearly were abortive poliomyelitis; others were less well defined; clinical diagnosis was impossible. Obviously, it was not possible in these families to delineate apparently healthy carriers of poliomyelitic virus. Perhaps this is further confounded in that the data, as might be expected, provide no constant relationship between number of household members and incidence of illness, however minor its manifestations.

These data, in consideration of some others previously reported,[1,2] have suggested that in certain milieu poliomyelitic virus can be implanted at the same time in many, if not all members of certain households. Some of the evidence has suggested that widespread seeding of virus in a household may occur more commonly in rural than in urban communities. This is not an inflexible rule, for in urban outbreaks, multiple familial cases have occurred.

Considering the available data, it would appear that poliomyelitic virus was seeded in a susceptible family unit in "all or one" fashion. The occurrence of poliomyelitic virus in one member, or independent onset of illness in two members, has suggested in the first instance exposure of the sick individual to virus in an experience that was not shared by remaining members in the household. In the second instance, independent onset of poliomyelitis in two or more members may be viewed as (a) exposure at separate sources, or (b) introduction of virus to susceptible members by the index case or an apparently healthy carrier.

Some Random Observations on the Presence of Virus in the Milieu of the Human Host

Human stools.—Five of the 10 stools collected from human cases at the end of May 1948 were tested in rhesus monkeys. None of the inoculated monkeys showed clinical

TABLE III

Detection of Poliomyelitis Virus in Sewage and Water in Harrison and Pottawattamie Counties, Iowa, 1948

Site of Collection	County	Amount Collected (Liters)*	Monkey No.	Inoculum cc.		Fate of Monkeys					Result
				IP	IN	Fever	Paralysis	Histology	Challenge	Passage	
Lynn Lake	Harrison	4	C-286	18.0	—	0	0	0	N.D.	N.D.	0
Crescent Creek	Pottawattamie	4	C-287	11.0	—	0	0	N.D.	+	N.D.	0
Pigeon Creek	Pottawattamie	4	C-289	20.0	3.0	+	+	+	N.D.	+	+
Spooner Ditch (Mondamin)	Harrison	4	C-291	10.0	3.0	0	0	0	N.D.	N.D.	0
Mondamin Sewer Outlet	Harrison	4	C-283	10.0	2.0	0	0	0	N.D.	N.D.	0
Missouri Valley Sewer Outlet	Harrison	4	C-288	18.0	4.0	+	+	+	N.D.	+	+

* Sedimented in the Sharples centrifuge
IP = Intraperitoneal route IN = Intranasal route C = Cynomolgus monkeys ND = Not done
Challenge strain = A strain of virus from a winter case of poliomyelitis in Kansas City

or histologic evidence of poliomyelitis. The remaining five stools were not tested for poliomyelitic virus.

Effluent sewage.—Effluent sewage was obtained at Mondamin and Missouri Valley. The sewer in Mondamin originated at a consolidated school (dismissed two weeks prior to collection); several households were also connected to the sewer. Effluent sewage was tested and found negative for poliomyelitic virus. Sewage from the town of Missouri Valley was discharged directly into Willow River. A single sample of sewage obtained on June 2, 1948, was tested and found positive for poliomyelitic virus. The data concerning these tests appear in Table III.

Water.—Water samples were collected at four sites: Crescent Creek, Pigeon Creek, Spooner Ditch and Lynn Lake. Crescent Creek and Pigeon Creek were fresh water streams. Spooner Ditch had a sluggish flow of water; its source water was from drainage ditches and several springs north of Mondamin. Lynn Lake is an impounded body of water, covering an area of 10 acres.

A water sample was collected from Crescent Creek as it passed the rear of a household containing a child sick with paralytic poliomyelitis. An open pit privy, used by members of the affected household, was situated four yards from the creek. A water sample from Pigeon Creek was collected at the junction of Pigeon and Crescent Creek. This was done because of the presence of sickness suspected to be poliomyelitis in addi-

TABLE IV

TESTS MADE FOR POLIOMYELITIS VIRUS IN BIRDS, FROGS AND FISH OBTAINED IN HARRISON AND POTTAWATTAMIE COUNTIES, IOWA, 1948

Material	Harrison County	No. Collected	Monkey No.	Inoculum cc.		Fate of Monkeys				Result
				IP	IN	Fever	Paralysis	Histology	Passage	
Sparrow	Mondamin	2	C-294	14.0	9.0	0	Weak l. arm & leg (27 d)	0	Neg.	Neg.
Swallow	Mondamin	3	C-290	15.0	12.0	?	Weak r. foot (10 d)	0	Neg.	Neg.
Blackbird	Lynn Lake	1	C-298	17.0	13.0	0	0	0		Neg.
Grackle	Mondamin (sewer outlet)	1	C-295	18.0	14.0	0	0	0		Neg.
Pigeon	Mondamin	2	C-297	15.0	13.0	0	0	0		Neg.
Frogs	Mondamin	3	C-296	15.0	3.0	0	0	0	—	Neg.
Catfish	Lynn Lake	2	C-300	17.0	15.0	0	0	0		Neg.
Carp	Lynn Lake	4	C-299	15.0	4.5	0	0	0		Neg.
Buffalo fish	Lynn Lake	1	C-301	17.0	15.0	0	0	0		Neg.

IP = Intraperitoneal route IN = Intranasal route d = day

tional households located in Crescent City. A water sample from Spooner Ditch, into which emptied sewage from Mondamin School, was obtained one hundred yards below the sewer outlet. Water was obtained from Lynn Lake because of unexplained death of many fish late in May.

The results of tests made on the four samples of water obtained in Harrison and Pottawattamie Counties appear also in Table III. The water obtained from Pigeon Creek contained virus in sufficient quantity to cause clinical and histologic evidence of poliomyelitis in a cynomolgus monkey. Each of the remaining three samples was negative in a single test.

Potential reservoirs of virus.—In the Iowa study flies were not obtained; the fact was tacitly accepted that flies laden with virus probably circulated in the areas studied. Birds, fish and frogs were obtained. A search was made for the presence of poliomyelitic virus in the gastrointestinal tracts of these animals. The results of the tests appear in Table IV.

The birds and frogs were obtained either on the premises of a family attacked by poliomyelitis or near open sewer conduits. The fish were obtained at Lynn Lake. Polio-

myelitic virus was not detected in the gastrointestinal tracts of any of the birds, frogs or fish. Two cynomolgus monkeys, inoculated respectively with extracts of the intestinal tract of sparrows and barn swallows, were found to have weakness of one or more extremities in the third and fourth weeks following inoculation. Histologic evidence of poliomyelitis was not found in these animals. CNS tissue emulsions prepared from these monkeys failed to cause illness in passage monkeys or in rodents. These tests have been considered negative for poliomyelitic virus.

Characteristics of Iowa strains of poliomyelitic virus.—Two strains have been studied. Cynomolgus monkeys inoculated with the original materials developed facial palsy with little weakness of the extremities. The first passage of one of the strains (Mo. V.) in rhesus monkeys resulted in appearance of facial palsy and weakness of the right leg on the 14th day. The second and third passage of this strain produced paralysis (facial and extremities) on the seventh and eighth days. The second strain (P. Cr.) has been passaged successfully also.

The symptom complex in cynomolgus monkeys was extremely mild. This is further attested to in the fact that virus was not detected in the stools of human cases. These tests were made in rhesus monkeys. There is the possibility that inactivation of virus took place in the stool specimens during transit to the laboratory.

Discussion

It has been stated that multiple cases of poliomyelitis in an affected household are uncommon. From time to time, reports have appeared on families widely attacked by the disease. The studies of Wickman,[5] Caverly,[6] and Paul, Salinger, and Trask[7] have brought into view minor illnesses, which are actually poliomyelitis; these illnesses not infrequently occur in additional members of a household attacked by poliomyelitis. Recent studies have pointed out the widespread distribution of virus in the family aggregate when the disease makes its appearance there.[1,2]

The present study, inferential in evidence presented, points out again that poliomyelitic virus not infrequently attacks a majority of members in certain family units. Obviously, not all patients have paralytic poliomyelitis. Due consideration must be allowed for the various symptoms manifesting themselves in the abortive forms of the disease. These have been adequately described elsewhere and will not be reconsidered here. The pertinent point is that frank and abortive attacks of poliomyelitis in these families occur at the same time or within a few days of each other. When these illnesses of simultaneous onset do occur, the circumstances suggest that these individuals shared in a common exposure.

A serious but not necessarily critical argument against the postulate of common source implantation of virus in all members of an affected household is the observation that poliomyelitic virus may be found in the throat a few days and in the feces of some individuals two or three weeks preceding the onset of illness. Precisely how many individuals carry virus during a period preceding illness, if any occurs, is not known. It is not a constant finding, as observed in the study of Zintek.[2] Limited extant information suggests that the number of individuals excreting virus prior to onset of illness may be few. If this is so, the fact that in many households multiple cases of poliomyelitis occur at the same time suggests that poliomyelitic virus is introduced to each member in a common vehicle. This has already been pointed out by Zintek[2] and Brown, Francis and Ainslie.[8]

Some earlier observations[9,10] indicate that poliomyelitic virus, having left the human

body, "circulates" in the environment of man. There is lack of convincing evidence that the existence of virus in various milieu is independent of human carriers. That there is excretion of virus in feces of frank and abortive cases of poliomyelitis for several weeks indicates clearly the opportunities of fecal contamination, not only of man's extraneous environment (i.e., sewage, soil, water), but for humans of immediate and perhaps remote association. The detection of poliomyelitic virus in creek water is indicative of pollution of the stream with virus originating in human feces.[11] There is a possibility that poliomyelitic virus can survive and multiply in other hosts. Among these are certain species of flies.[12] The observations of Ward and associates[13] that flies can deposit sufficient virus on food to produce a carrier state in chimpanzees indicate the potential danger to humans of food or drink contaminated by poliomyelitic virus.

Summary

In certain families poliomyelitis attacks many, if not all, members of the household. Not all members of the household develop paralytic poliomyelitis. The onset of illnesses among members occurs at the same time, suggesting a common exposure. The factors responsible for an intense common exposure of most, if not all, members in a household at risk are largely unknown.

In a search for poliomyelitic virus at extra-human sources in a rural epidemic, virus was detected in sewage and creek water. Poliomyelitis was not found in the entrails of birds, frogs or fish collected in the immediate areas of human cases of poliomyelitis.

Acknowledgment

The authors are indebted to Dr. Walter L. Bierring, Commissioner, State Department of Health, Des Moines, Iowa, for the privilege of studying this outbreak of poliomyelitis. Acknowledgment is made to Miss Olive Johnson, District Health Nurse, for obtaining most family histories. Mr. M. O. Nelson, Public Health Engineer, assisted the authors materially in the collection of extra-human specimens.

References

1. Wenner, H. A., and Tanner, W. A., Poliomyelitis in families attacked by disease. I. Distribution of virus in stool and oropharynx of members in households, Am. J. M. Sc. **216**:258, 1948.
2. Zintek, A. R., Rapid infection of family after introduction of poliomyelitis virus, Am. J. Hyg. **46**:248, 1947.
3. Trask, J. D., Vignec, A. J., and Paul, J. R., Isolation of poliomyelitis virus from human stools, Proc. Soc. Exper. Biol. & Med. **38**:147, 1938.
4. Howe, H. A., and Bodian, D., Untreated human stools as source of poliomyelitis virus, J. Infect. Dis. **66**:198, 1940.
5. Wickman, I., Acute poliomyelitis, New York, Nervous and Mental Disease Publishing Company, Nervous and Mental Monograph, Series 16, 1913.
6. Caverly, D. S., Preliminary report of epidemic of paralytic disease occurring in Vermont, in summer of 1894, Yale M. J. **1**:1, 1894.
7. Paul, J. R., Salinger, R., and Trask, J. D., Studies on epidemiology of poliomyelitis. I. Methods and criteria for detection of abortive poliomyelitis, Am. J. Hyg. **17**:587, 1933.
8. Brown, G. C., Francis, T., Jr., and Ainslee, J., Studies of distribution of poliomyelitis virus, V. Virus in familial associates of cases, J. Exper. Med. **87**:21, 1948.
9. Paul, J. R., Trask., J. D., and Gard, S., Poliomyelitis virus in urban sewage, J. Exper. Med. **71**:765, 1940.
10. Trask, J. D., Paul, J. R., and Melnick, J. L., Detection of poliomyelitis virus in flies collected during epidemics of poliomyelitis, J. Exper. Med. **77**:531, 1943.

11. Toomey, J. A., Takaes, W. S., and Weaver, H. M., Isolation of poliomyelitis virus from creek water by direct transmission to cotton rat, Am. J. Dis. Child. **70**:293, 1945.
12. Melnick, J. L., and Penner, L. R., Experimental infection of flies with human poliomyelitis virus, Proc. Soc. Exper. Biol. & Med. **65**:342, 1947.
13. Ward, R., Melnick, J. L., and Horstmann, D. M., Poliomyelitis virus in fly contaminated food collected at epidemic, Science **101**:491, 1945.

SPANISH ABSTRACT

Estudios de un Brote de Poliomielitis en Iowa con Referencia a Incidencia Familial y la Presencia de Virus en el Medio Extra-Humano Inmediato

Se hizo un estudio en una area rural del Oeste de Iowa para delinear la frecuencia de poliomielitis en ciertos hogares y la presencia del virus en un ambiente extra-humano.

En ciertas familias la poliomielitis ataca a muchos, si no a todos, miembros de la casa. No todos los miembros de casa desarrollan poliomielitis paralítica. El principio de las enfermedades entre los miembros ocurre al mismo tiempo, sugeriendo una exposición común. Los factores responsables para una exposición común intensa de la mayor parte, si no todos, de los miembros en una casa en peligro son bastante desconocidos.

En busca de virus poliomielítico en fuentes extra-humanas en una epidemia rural, se descubrió el virus en el agua de riachuelos y de albañal. No se encontró poliomielitis en las entrañas de los pájaros, ranas ni pescado recogidos en las inmediaciones de casos humanos de poliomielitis.

University of Kansas Medical Center

EVALUATION OF THE MUMPS SKIN TEST

By ALFRED L. FLORMAN, M.D., ALFRED E. FISCHER, M.D.,
AND RALPH E. MOLOSHOK, M.D.
New York City

ENDERS, Cohen and Kane[1] in 1945 reported that individuals who had had epidemic parotitis gave a tuberculin-like reaction following the intradermal inoculation of a small amount of an emulsion of the parotid gland from monkeys infected with mumps virus. Shortly thereafter the virus was adapted to the chick embryo by Habel.[2] He also demonstrated a good correlation between the skin reactions to virus grown in the chick allantoic sac and in the monkey parotid gland. Because of the greater availability of egg-grown virus, the wider use of this reaction then became possible.

Enders and co-workers[1,3] showed that in general the mumps virus skin reaction became positive several weeks following infection and that it might remain so for many years. They also showed that the majority of patients with positive skin tests had complement-fixing antibodies. Nevertheless, the two tests are not entirely parallel. Because of its greater persistence, the skin test would seem to be a more sensitive indicator of previous infection than the complement-fixation test. The chief exceptions to this generalization are young children in whom the skin reaction is often less striking. From their observations on many hundreds of adults and children, mostly in institutions and school, Enders, Kane, Maris and Stokes[3] concluded that persons exhibiting erythematous dermal reactions exceeding 10 mm. in mean diameter 48 hours after inoculation may, from a practical standpoint, be regarded as resistant to epidemic parotitis.

If the test should prove to be valid for determining resistance to epidemic parotitis, it should find wide application. When the disease appears in hospital wards and orphanages, it may permit the physician to safely shorten the duration of quarantine. Similarly, when it appears in a household in which the adults do not recall having had the disease and are concerned with the possibility of becoming infected, it may permit the physician to dispel that concern.

It is the purpose of the present communication to report the results of skin testing and follow-up in households intimately exposed to epidemic parotitis. Thus far only one other family group study, comprising a total of 92 individuals, has been reported.[3] Although the present study also represents a limited experience, it is offered as a contribution to the cumulative data needed for final evaluation of a diagnostic test.

METHOD OF STUDY

The present investigation was carried out from the spring of 1948 to the spring of 1949. It was planned as a cooperative project with the attending pediatric staff of the Mount Sinai Hospital. Whenever epidemic parotitis was diagnosed, all the members of the patient's household who remained

From the Pediatric Service and Division of Bacteriology of The Mount Sinai Hospital, New York City, N.Y.

Presented at the Clinical Research Meeting of the New York Academy of Medicine, June 1, 1949.
Dr. Florman's work was aided by a grant from the Sara Welt Foundation.
(Received for publication June 7, 1949.)

in contact with him were tested.* In addition to the reactions, the past history and subsequent fate in regard to epidemic parotitis of each contact was recorded, and an attempt made after several months to retest these individuals.

Most of the tests were made with a single batch of antigen† (Lab #7-1094-3A). It consisted of a mumps virus suspension made to be used as a vaccine, and was prepared as follows: Mumps-infected allantoic fluid was submitted to Sharples centrifugation. The precipitate was taken up in one fifth the original fluid volume. This partially purified and concentrated virus suspension was then inactivated with 0.05% formalin and preserved with 0.01% merthiolate®. For use in the skin test, this vaccine was diluted 1:10 in normal saline.

The tests were performed by injecting intradermally in the forearm 0.05 to 0.1 ml. of the antigen. The reactions were read in a bright light after 24 and 48 hrs. and the 2 maximum diameters of erythema were noted. A test was considered positive if the mean diameter of the reaction was 10 mm. or greater at either 24 or 48 hrs. These criteria are somewhat less stringent than those employed by others and may have resulted in including as positive some individuals whom others might have considered as negative or doubtful reactors.

Results

During the period covered by this report 40 households were studied. These were the source of 42 first cases of epidemic parotitis. The contacts of these patients included parents, siblings and domestics. It was possible to skin test 26 of the first cases and 109 of the contacts at least once. Eighty of these contacts were adults and 29 were children. Twenty-eight of these were retested several months later.

Reactions: The skin reactions appeared after 18 to 24 hours and were usually not as clearcut as a tuberculin reaction. The erythema was frequently faint and the edges indistinct. In some instances a test was positive after 24 hours, but obviously faded by 48 hours. In most instances, however, if the reaction was positive it took several days to fade completely.

It is still to be determined whether the faint reactions were due to an insufficient amount of antigen. The 1:10 dilution of vaccine selected for this study was suggested by Cabasso,[4] who supplied the material, as being a dilution which he had found to elicit a distinct erythema in most individuals with definite clinical history of epidemic parotitis.

Some individuals complained of pain immediately after the injection. The pain was of short duration and might have been due to a small amount of residual formalin in the antigen. An occasional adult who gave a strongly positive reaction developed pain or itching about the site of injection, induration, cellulitis and, in rare instances, a transient axillary adenitis.

Validity of the Test: All 26 of the first cases gave a negative reaction when tested during their acute illness. When 15 of them were retested several months later, 14 had become clearly positive and one questionably so.

Among the 109 contacts there were 60 with positive skin tests and 49 with negative tests. It is most significant that 11 of the 12 secondary cases of epidemic parotitis that occurred were among the 49 nonreactors (Chart 1).

No serologic tests were carried out with blood from the positive reactor who subsequently developed epidemic parotitis, and so it is not definitely known that she was a "false positive" reactor. However, it is of interest that Enders[5] feels that there is a some-

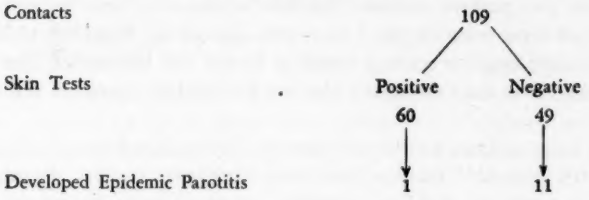
---

* The majority of the household groups which are the subject of this report were seen by the authors; a few were from the practice of Drs. Sidney Blumenthal and Herman Anfanger.

† The antigen employed was supplied by Drs. Cox and Cabasso of Lederle Laboratories.

CHART 1

Relation of Skin Reaction to Secondary Cases of Epidemic Parotitis

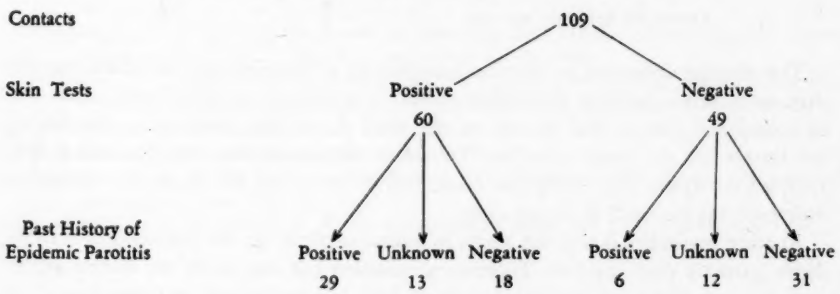


what larger number of individuals who give false positive reactions to egg-grown antigen than to that obtained from the monkey parotid gland.

Among the 109 contacts there were 35 who definitely recalled having had epidemic parotitis. The majority of these, 29, gave positive reactions to the test material. There were 49 of the contacts who thought that they had not had epidemic parotitis, and the majority of them, 31, had negative skin tests. However, 19 individuals who thought that they had not had the disease had positive reactions, and 13 of the 23 who were uncertain whether they had had it also gave positive skin tests (see Chart 2).

CHART 2

Relation of Skin Reaction to Past History of Epidemic Parotitis



The correlation of a positive skin test with the past history is in keeping with the findings of Enders, Kane, Maris and Stokes[3] and of Muntz, Powell and Culbertson.[6] The fact that one half of those who were uncertain of having had the disease and that more than one third of those who were certain that they had not had it also gave positive reactions is consistent with the known relatively high incidence of clinically inapparent epidemic parotitis.

Three household contacts out of 10 who were originally skin-test negative and were when retested after 6 to 12 months were found to have become skin-test positive. None of these individuals ever showed any clinical signs suggestive of mumps. Following his retest, one of these children who had developed a strongly positive test was exposed on two separate occasions to mumps, without contracting the disease.

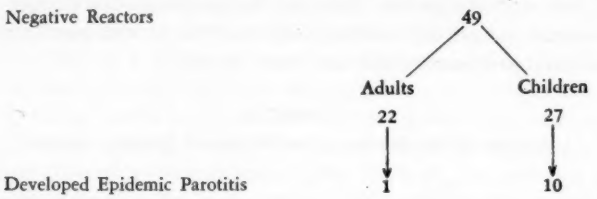
Relation of Age to Skin Reactivity: Enders, Kane, Maris and Stokes[3] have pointed out that in general children react less well to the antigen than do the adults. In our series there

were too few children to permit definite conclusions. However, our impression is in accord with already published observations. Among 29 contacts who were children, there were originally only two positive reactors. This low incidence is consistent with the fact that most of the children were in the 2 to 5 year age group. Retesting 15 first cases and 13 other originally negative reactors served to further this impression. The children gave smaller reactions than did most adults who had had epidemic parotitis in the more distant past.

Secondary Cases of Epidemic Parotitis Among the Negative Reactors in Relation to Age: Among the 109 household contacts there were 49 negative reactors. Twenty-two of these were adults and 27 were children under the age of 10 years. Yet of the 11 secondary cases of epidemic parotitis that occurred in this group, 10 were among the 27 children and only one among the 22 adults (Chart 3).

CHART 3

Secondary Cases of Epidemic Parotitis Among Negative Reactors in Relation to Age



This striking difference in apparent susceptibility of skin-test negative adults and children to epidemic parotitis deserves comment. A number of possible explanations must be considered. One is that because of the small size of the entire group the findings are merely due to chance selection. To aid in evaluating this, Mrs. Constance Percy analyzed the figures statistically. She found that there was but one chance in 150 that this difference was the result of chance alone.

Another possibility is that the adults by reason of their age are less susceptible to epidemic parotitis than children. There is no question but that when the disease appears among a population of skin-test negative adults in army camps or institutions,[5,7] the secondary case rate is high. Nevertheless, the available data on secondary case incidence among adults and children with the kind of exposure which exists in family units such as are seen in medical practice in New York City is still limited. In the only published series of contact cases of epidemic parotitis among family groups that were tested,[3] the authors were unable to find any greater susceptibility among the children than among the adults. However, in general, immature laboratory animals are more susceptible than older ones to a variety of other viruses.

A more likely explanation was suggested by Enders.[5] Since intimate exposure to an active case is necessary for contact infection, the observed differences might merely reflect a greater intimacy between the children who were ill and their siblings than between them and the adults. Most of the families studied lived in apartment buildings in which the parents and children slept in separate rooms. Consequently, the amount of contact might well have been less between parents and the ill child than between the siblings. Unfortunately, this study does not permit any definite statement in regard to this point.

This observation must therefore be left as an interesting but as yet incompletely understood lead for further study.

Conclusions

An intradermal test with formalin-inactivated egg-grown mumps virus was done on 109 household contacts of 42 cases of epidemic parotitis. Sixty of these individuals were skin-test positive and 49 negative. There were 12 contact cases of epidemic parotitis and 11 of them occurred among the nonreactors. There were 27 children who gave negative skin tests and they furnished 10 of the contact cases. The possible significance of this has been discussed.

The various types of reactions encountered have been described and the frequent occurrence of relatively faint reactions in children noted. The validity of the test was supported by an obvious correlation with the incidence of secondary cases, past history and the fact that patients who were originally skin-test negative were positive several months later.

It is concluded that the test is of value in determining susceptibility to epidemic parotitis. In view of the large number of clinically inapparent cases, the skin test should prove most useful in practice in removing unnecessary concern for infection by parents who do not recall having had the disease.

References

1. Enders, J. F., Cohen, S., and Kane, L. W., Immunity in mumps. II. Development of complement-fixing antibody and dermal hypersensitivity in human beings following mumps, J. Exper. Med. **81**:119, 1945.
2. Habel, K., Cultivation of mumps virus in developing chick embryo and its application to studies of immunity to mumps in man, Pub. Health. Rep. **60**:201, 1945.
3. Enders, J. F., Kane, L. W., Maris, E. P., and Stokes, J., Jr., Immunity in mumps. V. Correlation of presence of dermal hypersensitivity and resistance to mumps, J. Exper. Med. **84**:341, 1946.
4. Cabasso, V., Personal communication to the authors.
5. Enders, J. F., Personal communication to the authors.
6. Muntz, H. H., Powell, H. M., and Culbertson, C. G., Mumps vaccine: Studies in human volunteers, J. Lab. & Clin. Med. **34**:199, 1949.
7. Gordon, J. E., and Heeren, R. H., Epidemiology of mumps, Am. J. M. Sc. **200**:412, 1940.

Spanish Abstract

Avaluación del Análisis de Piel de las Parótidas

Se hizo un ensayo intradermal con virus de parótidas crecidas de huevos inactivos con formalina en 109 contactos de casa de 42 casos de parótidas. Sesenta de estos individuos tuvieron un análisis de piel positivo y 49 negativo. Hubieron 12 casos de parótidas de contacto y 11 de ellos ocurrieron entre los no reactores. Hubieron 27 niños que tuvieron análisis de piel negativo y ellos proporcionaron 10 de los casos de contacto. Se trata el posible significado de esto.

Se han descrito los varios tipos de reacciones que se han encontrado y se ha notado la ocurrencia frecuente de reacciones relativamente ligeras en los niños. La validez del ensayo fué colaborada por una correlación obvia con la incidencia de casos secundarios, la historia pasada y el hecho de que los pacientes que tuvieron originalmente ensayo de piel negativo tuvieron uno positivo algunos meses más tarde.

Se concluye de que el análisis es de valor para determinar susceptibilidad a parótidas. En vista del gran número de casos clinicamente inaparentes, el análisis de la piel debe de ser muy útil en la práctica para remover preocupación innecesaria de infección de los padres que no se acuerdan haber tenido la enfermedad.

Fifth Avenue and One Hundredth Street

NONLIPOID RETICULOENDOTHELIOSIS (LETTERER-SIWE'S DISEASE)

By EDWARD HAVARD, M.D., LELLAND J. RATHER, M.D., AND HAROLD K. FABER, M.D.
San Francisco

SINCE Letterer's[1] first description in 1924 of aleukemic reticuloendothelial hyperplasia in a child, about 30 similar cases have been reported or referred to in the literature, the majority within recent years, probably reflecting an expanding knowledge and interest in the reticuloendothelial system and its disorders. These reports show a considerable variation in individual cases in respect to age, nature of onset, type and severity of symptoms, laboratory findings, course, and gross and histopathologic alterations. For this reason and because the total number of cases is still small, another case showing some typical and some unusual features is presented in detail.

CASE

J. F., a 15 mo. old white American girl, entered Stanford University Hospital for unexplained anemia. She had been entirely well until 2 mo. before entry, when she developed a severe upper respiratory tract infection with otitis media. The acute symptoms subsided in about 2 wk., but she remained tired, lethargic, restless, irritable and pale, and her abdomen became enlarged. She developed an obstinate dermatitis of the scalp. A week before entry the eyelids became swollen and 2 days later the legs. Examination of the urine was normal. Blood count showed RBC 1.9 million, Hgb. 3 gm./100 cc., and WBC 2.8 thousand, with a normal differential count. A blood transfusion resulted in a rise to 2.9 million RBC and 8.2 gm./100 cc. of Hgb. Three days before entry a fine petechial rash appeared over the body. On the day before entry the blood count had again fallen to 2.05 million RBC and 5.8 gm./100 cc. Hgb.

Past history revealed that the mother's health during the pregnancy was normal except for asthma. Patient was the first born of nonidentical twins. Vertex delivery without anesthetic followed a 2 hr. labor. Condition at birth was good and the weight was 2.9 kg. Physical and mental development was normal and there had been no previous illnesses. Diet had always been adequate except for the omission of any form of vitamin D. No immunizations had been given.

Family history revealed that the mother had asthma and the father, migraine. The twin sister and a brother 12 yr. of age, were perfectly well. No family history of illness similar to that of the patient was elicited.

Examination showed the patient to be a well-developed and well-nourished girl who was irritable, pale and obviously very ill (see fig. 1). Temperature was 39.7° C. Pulse was 108/min. and respirations 24/min. Height, weight and head and chest circumferences were within normal limits, but the abdominal circumference was 5 to 7.6 cm. greater than average. A widespread fine petechial rash was especially prominent on the chin, back, diaper area and both axillae. There was also a severe weeping, erythematous dermatitis of the scalp, axillae, chin, neck creases and groins. Moderate soft edema of eyelids and legs below the knees was present. Posterior cervical and posterior auricular nodes were moderately, anterior cervical, axillary and inguinal nodes were slightly enlarged. No bony abnormalities were felt. Fundi were normal except for unusual pallor of discs and retinae; pupils and extraocular movements were normal; there was no exophthalmos. Teeth, gums and oral mucosa were normal. Heart was moderately enlarged to the left; there was a grade 1-2 harsh blowing systolic murmur, heard over the entire precordium, especially at the apex; diastole was clear. Lungs were

From the Departments of Pediatrics and Pathology, Stanford University School of Medicine, San Francisco, Calif.

(Received for publication July 6, 1949.)

clear. Abdomen was moderately protuberant and tense, without fluid wave, venous distension, tenderness or apparent pain. Spleen, palpable 2.5 cm. below the level of the umbilicus, was firm and smooth. Liver, felt 5 cm. below the umbilicus, was also firm and smooth. Genitalia were normal except for moderate soft labial edema. Reflexes were physiologic.

Laboratory findings on entry revealed a blood count of 2.65 million RBC, 7.0 gm./100 cc. of Hgb., and 1.8 thousand white cells (29% leucocytes of which 16% were banded, 66% lymphocytes, 5% monocytes and 2% nucleated red cells). Color index was 0.85; packed cell volume, 18%; mean corpuscular volume, 68 cubic micra (normal 80-94); mean corpuscular hemoglobin, 26.4 micro-micrograms (normal 27-32); mean corpuscular Hgb. concentration, 38.8% (normal 33-38%).

FIG. 1. Two days before death. Note purpuric rash on forehead, axillae and pubic area; facial edema and abdominal distention, latter due to great enlargement of liver and spleen and to massive ascites.

There were 1.6% reticulocytes and 12,350 platelets/cmm. The urine contained only occasional white cells and a rare red cell. Tuberculin and histoplasmin skin tests were negative. Wassermann test was negative. Blood cholesterol was 160 mg./100 cc., blood urea was 30 mg./100 cc. and plasma proteins were 5.0 gm./100 cc. Blood culture revealed a coagulase-positive Staph. aureus which was not inhibited by penicillin 0.4 u./cmm. Chest Rngm. showed generalized cardiac enlargement and some soft mottling in both upper lung fields. Skull Rngm. revealed a 4x3 mm. radiolucent area in the L. frontal squama (considered by the radiologist too small to be diagnostic of bone involvement). Rngm. of the ribs and vertebrae were normal; long bones appeared somewhat shorter, thicker and denser than usual, but in other respects were normal.

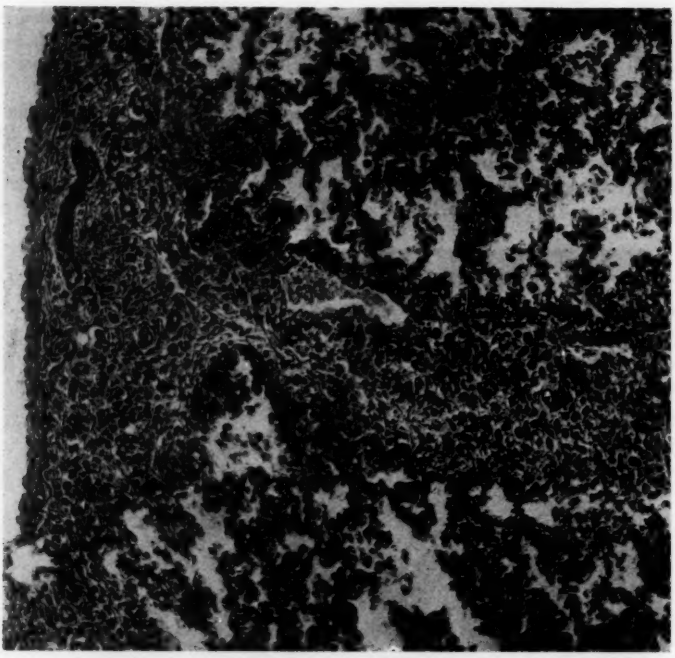


FIG. 3. Lung (×100).

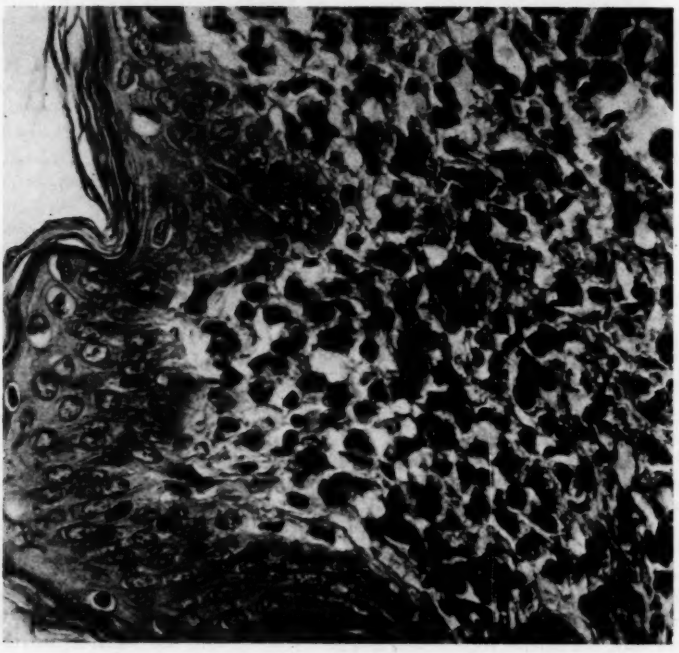


FIG. 2. Skin (×100).

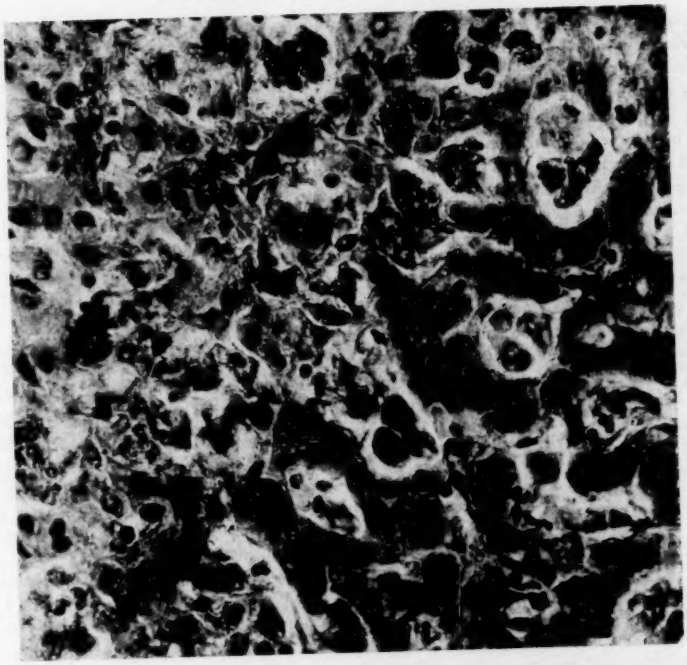


FIG. 3. Liver (×400).

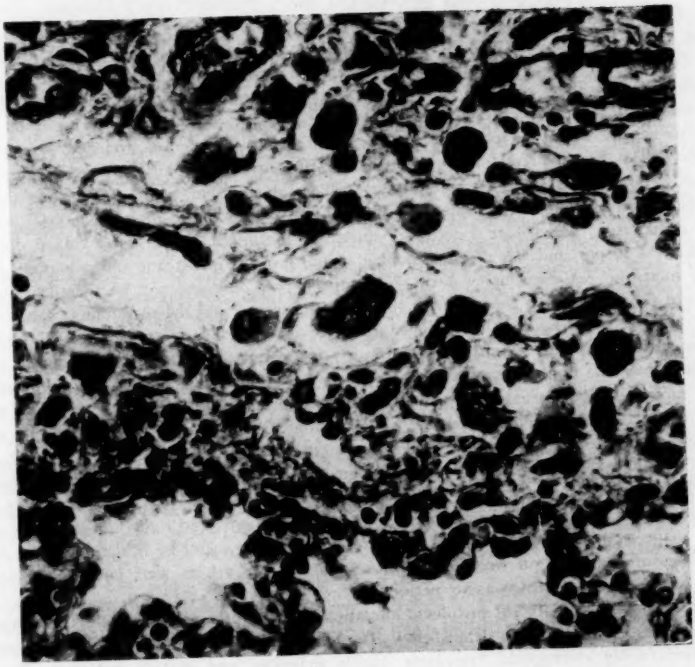


FIG. 4. Lung (×400).

Course was progressively downhill. During most of the 33 day period between hospital entry and death, she had a swinging fever, with late afternoon peaks of 38° to 38.8°C. Purpura increased and later involved palms and soles. Dermatitis of the scalp became more severe despite appropriate local treatment. Face (especially the eyelids), hands and feet became notably edematous. Abdomen became markedly distended due mainly to progressive enlargement of liver and spleen; liver extended to 2.5 cm. below the iliac crest and the spleen reached the iliac crest; both organs remained firm, smooth and nontender. Anemia, leukopenia and thrombocytopenia responded only slightly and briefly to repeated transfusions with regular bank blood, fresh donor blood and red cell concentrate. Several careful smears of peripheral blood failed to reveal any immature or otherwise abnormal cells; a relative and actual neutropenia persisted, the neutrophil count falling to 195/cmm. on 2 occasions, while the total white count fell to 1.0 thousand/cmm. Biopsy of a cervical node revealed an intact lymphoid architecture, slight thickening of the capsule and moderate hyperplasia of the reticuloendothelial cells; no lipoid storage, infiltration of giant cells or eosinophiles or granuloma formation was observed. Diagnosis was "lymph node hyperplasia, reticuloendothelial." She was given penicillin on entry because of fever and leukopenia and this was continued throughout her course. Sulfadiazine was given also after 2 wk. because of persistent fever and this was also continued throughout her course. Repeated blood cultures, with the exception of the first which showed Staph. aureus, were sterile. Three weeks after admission blood cholesterol was 120 mg./100 cc. A week later she was in definite respiratory distress, with a rate of 90/min. At this time an abdominal fluid wave was elicited and on paracentesis 1000 cc. of moderately cloudy pale yellow fluid were removed, providing some relief from the dyspnea. It was necessary to repeat the paracentesis 2 days later, when 900 cc. of similar fluid were removed. During the next few days the child became progressively less responsive, finally comatose, and died 5 wk. after admission.

Autopsy (Dr. Alvin Lewis): *Gross:* body weighed 15.9 kg. and was 76 cm. long. Abdomen was protuberant. *Skin:* A brown maculopapular rash was present on the trunk and head. It was almost confluent over the scalp, bridge of the nose, ears and axillae; thinly scattered over the abdomen and back, and confluent again in the pubic region. *Peritoneal cavity and abdominal viscera:* A midline incision disclosed edematous subcutaneous tissue. Peritoneal cavity contained 120 cc. of clear colorless fluid. Mesentery and omentum were edematous. Liver weighed 720 gm. Its surface was smooth and red-brown with scattered yellowish subcapsular markings, about 2 mm. in diameter. Dome of liver on left side contained an irregular grayish area, about 1 cm. in diameter, bordered by a narrow red zone. This appeared to be an infarct. Cut surface of liver showed normal lobular markings and small irregular grayish translucent areas, without obvious zonal distribution. Gallbladder, extra-hepatic ducts and portal system were not remarkable. Spleen weighed 480 gm. and extended almost to the iliac crest on the left side. Its smooth dark red surface was interrupted by several slightly bulging yellow zones, the largest of these about 4 cm. across. On section they appeared to be infarcts. Remainder of splenic pulp was dark red and firm. Malpighian follicles were not clearly demarcated. There were 2 accessory spleens at the hilum, the largest 1 cm. in diameter. Pancreas weighed 50 gm. and was distinctly lobulated and firm. Peripancreatic and mesenteric lymph nodes were numerous, enlarged up to 1 cm. in diameter, pale pink and wet on their cut surfaces. Adrenals were surrounded by a thick grayish tissue which merged into the surrounding fat. Kidneys weighed 60 gm. each. Their capsules stripped easily and exposed surfaces were pale brown and smooth. Cut surfaces showed distinct demarcation of cortex and medulla. In the peripelvic region and extending down the ureter there was yellowish gray tissue which did not look like ordinary fat. Two small submucosal hemorrhages were seen in the midportion of the left ureter and one in the bladder, which was otherwise not remarkable, at the trigone. *Thoracic viscera:* Both pleural cavities contained 50 cc. of clear colorless fluid and the pericardial sac contained 8 cc. of similar fluid. Thymus did not appear enlarged. Heart weighed 80 gm. and was not remarkable except for a peppering of all the epicardial surfaces with red petechiae. Pleural surfaces were smooth, but there were scattered petechiae on the parietal pleura. Left lung weighed 100 gm., and right 120 gm. They maintained their shape well on section. Cut surfaces were moist and the major bronchi contained a frothy fluid. No zones of consolidation were present. Remainder of the viscera were not remarkable. An examination of the cranial contents was not performed.

Microscopic Findings: Significant histologic alteration was the presence of a cellular infiltrate in the organs and tissues, described in detail below. The type cell of the infiltrate was a large mononuclear cell with faintly eosinophilic cytoplasm, clearly delimited and without processes. The cell

diameters ranged from 15 to 25 μ and the nuclear diameters from 10 to 15 μ. The nuclei were round or oval, irregularly folded or indented, and contained finely dispersed chromatin. Nucleoli were rarely seen and mitotic figures were not present. Evidence of phagocytosis, in the form of intracytoplasmic vacuoles or particles, was frequently present, though not seen in a majority of the cells. Sudan IV and Best's carmine stains for fat and glycogen, respectively, in the type cell, were negative. In addition to the mononuclear cells there were multinucleated giant cells with the same general cytoplasmic and nuclear structure. In some of the tissues, particularly the pancreas and the capsule of the accessory spleen, there was an admixture of cells, predominantly lymphocytes, with fewer plasma cells and rare eosinophiles. Fibroblasts and thin strands of collagen were present in these zones, but were not characteristic of the infiltrate elsewhere. Reticulum fibrils were not demonstrated in relation to the type mononuclears, except in these zones of fibroblastic proliferation. *Skin:* A section through one of the macular lesions showed an intact layer of epidermis. Beginning immediately beneath the basal layer there was an infiltration of large mononuclear cells (fig. 2) and a few lymphocytes. Well-preserved extravascular erythrocytes were present and fairly numerous in some areas but only a few granules of hemosiderin were seen. *Heart and Aorta:* There was a minimal infiltration of the epicardium and of the aortic adventitia by the type mononuclears. The muscle fibers appeared normal, though the bundles were somewhat widely separated. *Lungs:* Subpleural and intralobular lymphatic channels were greatly distended by large mononuclear cells (fig. 3) with a scattering of small lymphocytes. A few of the multinucleated variants (fig. 4) of these cells, but no eosinophiles, were present. Alveolar septae appeared thickened and contained large mononuclear cells, some of which were free in the alveolar spaces. *Liver:* Sinusoids were crowded with mononuclear cells among which the Kupffer cells did not appear as a distinct group. These mononuclears showed evidence of very active phagocytosis (fig. 5), far more than in any other organ or tissue with the exception of the spleen. They contained bits of erythrocytes and leucocytes but chiefly large amounts of fine granular brown pigment which gave the Prussian blue reaction for iron. No iron containing pigment was seen in the liver parenchymal cells. Scattered throughout the sinusoids were foci (fig. 6) of stem cells, immature granulocytes and occasional megakaryocytes. Immature red cells were identified with difficulty. *Spleen:* The Malpighian follicles were altered by the almost total disappearance of lymphocytes and deposition of fibrous tissue around the central vessels. Lying within the fibrous strands were large mononuclear cells containing hemosiderin granules. Elsewhere splenic sinusoids and pulp were crowded with mononuclear cells containing large quantities of granular pigment identifiable as iron-containing by the Prussian blue reaction. Foci of myelopoiesis, similar to those in the liver, were scattered throughout. Typical areas of infarction were present. *Accessory Spleen:* The structure was similar to that of the spleen. The capsule, however, was thickened by layers of dense collagenous tissue and was adherent to the pancreas. *Pancreas:* Connective tissue uniting the accessory spleen to the pancreas was loosely fibroblastic and infiltrated by type mononuclear cells, lymphocytes and a few plasma cells and eosinophiles. Pancreatic islets and acini were not altered but the fibrous septae of the organ were greatly enlarged by a cellular infiltrate, predominantly large mononuclear but with more plasma cells and eosinophiles than were seen elsewhere. *Kidneys:* Glomeruli and tubules appeared normal. Peripelvic connective tissue was infiltrated by type mononuclear cells, plus a few lymphocytes. *Adrenals:* Cortex and medulla appeared normal but the surrounding connective tissue was infiltrated by large mononuclears and lymphocytes. A few of the type cells showed evidence of phagocytosis. *Lymph Nodes:* Lymph sinuses were filled with large mononuclears. Lymph follicles were decreased in number and germinal centers seemed to be replaced by type large mononuclear cells. *Gastrointestinal Tract:* Lymphoid follicles were not present in the ileum. Mucosa was infiltrated by large numbers of type mononuclear cells plus a scattering of lymphocytes (fig. 7). *Bone Marrow:* There were large foci of replacement of the cellular marrow of the vertebrae (fig. 8) and ribs by type mononuclear cells. Remaining cellular marrow was not studied quantitatively, but did not appear significantly altered. The bone spicules were not altered. *Parathyroid:* There was a remarkable infiltration by large mononuclear cells with more of the giant multinucleated forms (fig. 9) than were seen in any other tissue. *Thyroid:* Follicles were uniform, colloid-filled, and lined by cuboidal epithelium.

Anatomic Diagnoses: (1) Hyperplasia and infiltration of large mononuclear phagocytic (reticuloendothelial) cells in lungs, liver, spleen, lymph nodes, adrenal, parathyroid, intestinal submucosa, pericardium, skin, pancreas, aortic adventitia, bone marrow, periureteral, peripancreatic and periadrenal fat tissue; (2) myeloid metaplasia of liver and spleen; (3) multiple infarcts of liver and

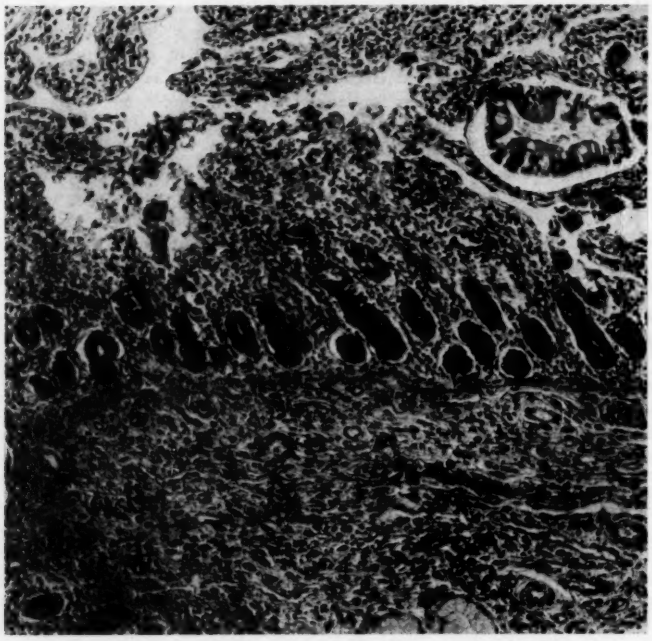


FIG. 7. Small bowel (×100).

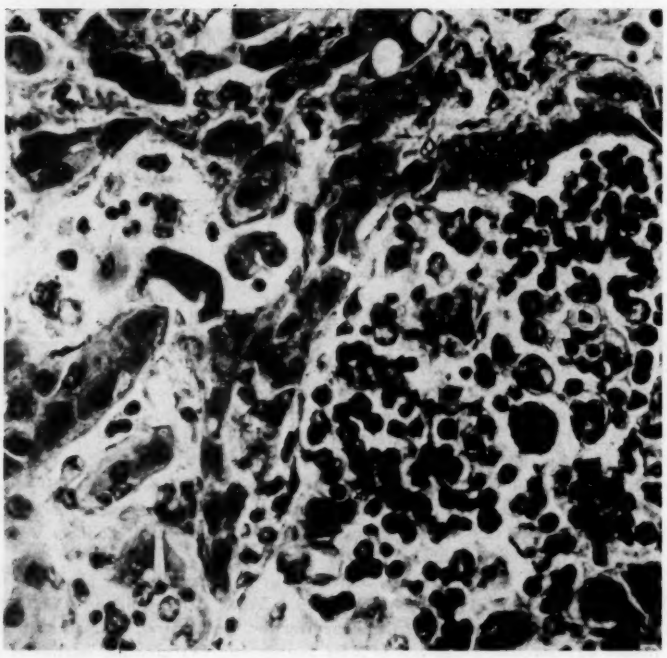


FIG. 6. Liver (×400).

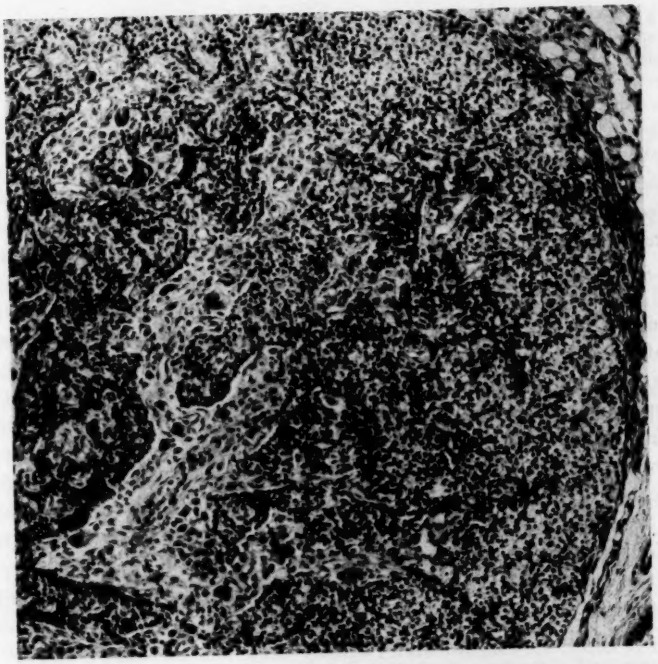


FIG. 9. Parathyroid (×100).

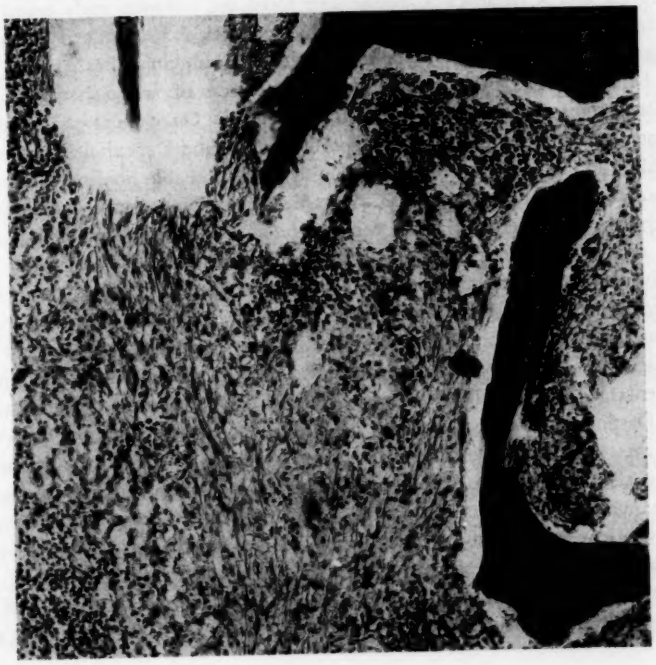


FIG. 8. Vertebral marrow (×100).

spleen; (4) petechial hemorrhages of skin, epicardium and parietal pleura; (5) atrophy and fibrosis of splenic lymphoid follicles; (6) mild fibrosis of pancreas and periadrenal tissue; (7) accessory splenic tissue.

Discussion

Nonlipoid reticuloendotheliosis (aleukemic reticulosis, Letterer-Siwe's disease) was first accurately described by Letterer[1] in 1924; however, Borissowa[2] in 1903 probably reported the first cases, though she believed they represented an early stage of splenic anemia (Banti's disease). Siwe[3] in 1933 grouped the previously reported similar cases into a definite clinocopathologic entity and listed these characteristics: (1) enlargement of the spleen and liver; (2) hemorrhagic diathesis, especially petechiae and purpura; (3) generalized lymphadenopathy of mild to moderate degree; (4) progressive anemia with a usually normal leukocyte count; (5) nonhereditary, nonfamilial occurrence, exclusively in infants and young children, with unknown etiology, fatal prognosis and variable duration (from a few weeks to several years); (6) localized skeletal tumors; (7) generalized hyperplasia of the reticuloendothelial cells with focal tumorous proliferations, especially in the spleen, liver, lymph nodes, thymus, skin and bone marrow, often showing a hemorrhagic tendency but no lipoid storage. A large majority of the cases occur between the ages of 12 and 30 months, although similar clinical and histopathologic pictures have been described in adults. Our case is the only one reported in a twin; the other twin in this instance is apparently perfectly well.

The onset is usually insidious, often following or associated with an upper respiratory or other infection; frequently the patient is brought in because an apparently ordinary illness persists or fails to respond to appropriate therapy. Weakness, pallor, fatigue, irritability, anorexia and a tendency to bruise and bleed are common early manifestations. There is frequently slight to moderate fever; Dameshek's[4] patient had an undulating fever suggestive of the Pel-Ebstein type in granuloma (Hodgkin's disease). The petechial rash may be extensive, especially prominent in the areas of friction, such as the neck folds, axillae, groins and flexion creases of the extremities. Our patient had rather marked petechiae on the palms and soles; a case reported by Abt and Denenholz[5] showed palmar petechiae also, and a patient of Lane and Smith[6] with probable nonlipoid reticuloendotheliosis had purpura of the palms and soles. A scaly, yellow, crusted, inflamed eczematoid or seborrhea-like dermatitis has been reported in several cases, being especially prominent on the scalp and refractory to treatment. Soft tissue swellings over areas of bony involvement are occasionally seen. Edema is an unusual finding; there was considerable edema of the face, legs and genital labia in our patient; Lichty[7] mentioned ankle edema in his case; Van Creveld and Ter Poorten[8] reported a swollen face in their patient. Ours is the only reported instance of ascites. The spleen and liver are mildly to extremely enlarged, are usually nontender, and present a uniform and firm surface to palpation. Dyspnea is common and may be due to encroachment on the thorax by the abdominal mass; the anemia or the involvement of the lung parenchyma by the disease process may also contribute to the dyspnea. Anemia is constant and may be severe; it varies from normochromic to slightly hypochromic; it tends to progress and usually responds only briefly to transfusions and poorly to hematinics. Reticulocyte counts have been normal or slightly increased in the few determinations reported. There may be moderate leukocytosis, but slight to moderate leukopenia is more common, and the reduction is usually in the neutrophiles; our patient's count with 1000 white cells and 200

neutrophiles/cmm. is the lowest recorded. Occasionally a slight monocytosis is found, but there have been no instances of significant eosinophilia. Thrombocytes may be normal or even elevated (Siwe's[3] patient had 1.4 million platelets/cmm.), but as a rule there is mild to severe thrombopenia; the 12.5 thousand count of our patient is by far the lowest. Blood cholesterol is usually normal but is occasionally slightly elevated. Signs of liver dysfunction are rare; a patient with jaundice is described in the Case Records of the Massachusetts General Hospital;[9] a patient of Wallgren[10] developed jaundice, bile in the urine and clay-colored stools (however, Wallgren believed this represented an associated infectious hepatitis, since there were several neighboring cases); our patient had low serum protein concentration. Roentgenograms of the bones have revealed in several cases rarefied or cystic areas which resemble those seen in essential xanthomatosis (Hand-Schüller-Christian disease), though generally less marked. These are commonest in the flat bones of the skull and pelvis and also in the ribs, but apparently can occur in other bones as well. Roentgenograms of the lungs occasionally demonstrate perihilar or diffuse parenchymatous soft infiltration of a nonspecific character, resembling that seen in pneumonoconiosis or miliary tuberculosis.

Anatomically, nonlipoid reticuloendotheliosis is characterized by enlargement of the superficial and deep lymph nodes, often with one or more chains being more involved than the rest; the nodes are of normal or softer consistency, and the color varies from light grayish pink to brown or deep red; occasionally hemorrhagic or necrotic areas are found; the cut surface is frequently granular in appearance. The liver and spleen generally retain their shape and are usually of normal consistency; on the cut section the normal pattern is indistinct and small grayish yellow nodules are scattered throughout; the liver is sometimes fatty in appearance; occasionally the lobular markings of the liver are accentuated due to the hyperplasia in the sinusoids. The bone marrow is usually abundant, often red or pink, and either firm or soft; occasionally cysts or rarefied areas of the bone are found. Generalized petechial or purpuric rash of the skin and of the submucous and subserous tissues is usually present, subepicardial hemorrhages being common. The thymic architecture is often indistinct and there may be many small abscess-like areas. The lungs are occasionally heavy and moist, with varying degrees of diffuse pneumonia; a few cases have had small collections of clear pleural fluid.

Histologically, all involved areas show the same process, a widespread hyperplasia of large mononuclear cells. These cells are large, measuring at times 30 to 50 μ across; they may be irregularly round, oval or polyhedral. Several investigators have reported indistinct cell borders, with protoplasmic projections forming a reticulum or meshwork; however, in other cases and in the present case the cell borders were distinct and without projections. The cytoplasm is pale and is usually faintly acidophilic; there is no lipoid storage as a rule, though lipoid droplets are occasionally found in small amounts, especially in cases of longer duration. The single nucleus is round, oval or kidney shaped; it may be vesicular and it is usually eccentrically placed; the nuclear membrane is generally distinct. Phagocytic multinucleated giant cells are frequently found, in some instances similar to the Reed-Sternberg cells of Hodgkin's disease. Infiltrations of eosinophilic cells, especially eosinophilic leukocytes, have been observed by several investigators. Yellowish brown pigment, both intracellular and extracellular, has been described, and in some cases this has been shown to be hemosiderin. The macroscopic lesions are formed by accumulations of the mononuclear cells, and widespread hyperplasia and infiltration are re-

sponsible for the architectural distortion seen in the lymph nodes, spleen, liver and elsewhere.*

As is true of the other reticuloendothelial diseases, the etiology of nonlipoid reticuloendotheliosis is unknown. In the majority of cases the onset follows or is ushered in by infection, especially otitis media, tonsillitis, upper and lower respiratory disease, and occasionally gastrointestinal or urinary infection. Some observers have therefore felt that infection is an important if not the dominant etiologic factor, and on this basis have divided otherwise indistinguishable cases into infectious and noninfectious groups. Wallgren[10] and others find such division unjustifiable and point out that in virtually none of the reported cases could infection be excluded, though repeated cultures in many of the cases have consistently failed to demonstrate an etiologic agent. The possibility of a viral infection cannot be excluded, but no direct evidence for it has been discovered. Rowland[11] and some others have considered an error of lipoid metabolism as the primary disorder in all reticuloses and have felt the reticuloendothelial hyperplasia was a secondary phenomenon. More recently, however, Wallgren,[10] Imler,[12], Mallory[13] and Klemperer[14] have concluded that the primary defect is a hyperplastic response of the reticuloendothelial system to some unknown stimulant, and believe that lipoid accumulation is incidental to the reticuloendothelial dysfunction.

In recent years it has been pointed out that eosinophilic granuloma, essential xanthomatosis and nonlipoid reticuloendotheliosis are closely related. Wallgren,[10] Gross and Jacox,[15] Mallory,[13] Jaffe and Lichtenstein,[16] Imler,[12] Bartels[17] and others have stressed this interrelationship. The three diseases may represent more or less definable grades of a common pathologic process, in which nonlipoid reticuloendotheliosis is the most acute and severe and eosinophilic granuloma is the most mature and benign. Certainly a large proportion of the cases of each clinical type show histologic features overlapping the other types and an individual case may show distinctly different stages in different parts of the body. Where this occurs the progression from one stage to another is characterized by a gradual accumulation of cholesterol or its esters within the reticuloendothelial cells, by a tendency to form lesions of increasing size, and by an irregularly increasing infiltration of eosinophilic cells and giant cells. With respect to these hypotheses, it should be recalled that histologic, or even histogenetic, interrelationships do not necessarily imply identity of etiologic agents.

Summary

A case of nonlipoid reticuloendotheliosis (Letterer-Siwe's disease) with autopsy is reported. The relationship to essential xanthomatosis (Hand-Schüller-Christian) and to eosinophilic granuloma is discussed. Unusual features of our case, classical in other respects, were the severe leukopenia and thrombocytopenia, the presence of severe edema and ascites, associated with hypoproteinemia.

References

1. Letterer, E., Aleukämische Retikulose, Frankfurt Ztschr. f. Path. **30**:377, 1924.
2. Borissowa, A., Beitrage zur Kenntnis der Bantischen Krankheit und Splenomegalie, Virchow's Arch. f. path. Anat. **172**:108, 1903.
3. Siwe, S., Die Reticuloendotheliose—ein neues Krankheitsbild unter den hepatosplenomegalien, Ztschr. f. Kinderh. **55**:212, 1933.

* These mononuclears are generally referred to as "reticuloendothelial cells." Without accepting all of the implications of this term, it is used in this paper for the sake of uniformity.

4. Dameshek, W., Acute monocytic (histiocytic) leukemia, Arch. Int. Med. **46**:718, 1930.
5. Abt, A., and Denenholz, E., Letterer-Siwe's disease, Am. J. Dis. Child. **51**:499, 1936.
6. Lane, C., and Smith, M., Cutaneous manifestations of chronic (idiopathic) lipoidosis (Hand-Schüller-Christian disease), Arch. Dermat. & Syph. **39**:617, 1939.
7. Lichty, D., Lipoids and lipoid diseases, Arch. Int. Med. **53**:379, 1934.
8. Van Creveld, S., and Ter Poorten, F., Infective reticulo-endotheliosis chiefly localized in lungs, bone marrow, and thymus, Arch. Dis. Childhood **10**:125, 1935.
9. Case Records of the Massachusetts General Hospital, New England J. Med. **226**:392, 1942.
10. Wallgren, A., Systemic reticuloendothelial granuloma: Non-lipoid reticuloendotheliosis and Schüller-Christian disease, Am. J. Dis. Child. **60**:471, 1940.
11. Rowland, R., Xanthomatosis and reticulo-endothelial system, Arch. Int. Med. **42**:611, 1928.
12. Imler, A., Reticulo-endotheliosis, Am. J. Roentgenol. **56**:343, 1946.
13. Mallory, T., Pathology of diseases of bone, New England J. Med. **227**:955, 1942.
14. Klemperer, P., Reticulo-endothelial system, Marquette M. Rev. **11**:243, 1946.
15. Gross, P., and Jacox, H., Eosinophilic granuloma and certain other reticulo-endothelial hyperplasias of bone, Am. J. M. Sc. **203**:673, 1942.
16. Jaffe, H., and Lichtenstein, L., Eosinophilic granuloma of bone, Arch. Path. **37**:99, 1944.
17. Bartels, J., Over het eosinophiele granuloom der beenderen, en het verband hiervan met de ziekte van Hand-Schüller-Christian en de ziekte van Abt-Siwe-Letterer, Nederl. tijdschr. v. geneesk. **91**:2578, 1947.

SPANISH ABSTRACT

Reticuloendoteliosis No Lipoide (Enferded Letterer-Siwe)

Se presenta un caso de reticuloendoteliosis no lipoide (enfermedad de Letterer-Siwe) en una niñita de 15 meses de edad, mostrando las características clásicas de hepatosplenomegalia, anemia, leucopenia, trombocitopenia, diatesis hemorrágica, linfadenopatía generalizada, fiebre y una dermatitis del cuero cabelludo parecida a la seborrea. Descubrimientos raros fueron la leucopenia y trombocitopenia y la presencia de edema marcada y ascitis, asociados con hipoproteinemia. La relación con xantomatosis esencial (enfermedad Hand-Schüller-Christian) y granuloma eaosinofílica se trata.

Stanford University School of Medicine

NEPHROTIC SYNDROME

I. Natural History of the Disease

By LEWIS A. BARNESS, M.D., GRETCHEN H. MOLL, M.D.,
AND CHARLES A. JANEWAY, M.D.
Boston

THE nephrotic syndrome, which occurs mainly in children, is manifested by edema, albuminuria, lipemia and hypoproteinemia, usually with relatively normal levels of nonprotein nitrogen in the blood and relatively normal blood pressure, and is characterized by a chronic course with exacerbations, remissions and, in many instances, eventual recovery. It is the purpose of this paper to review the natural history of this disease, as it has been observed in this clinic, as a background for present and projected studies on its pathogenesis and treatment. Particular emphasis has been placed on establishing criteria which might assist prognosis and on identifying the factors which contribute to an unfavorable outcome.

Although similar studies have been made in other clinics,[1-4] the extensiveness of this material, possible geographic differences, and an impression that the prognosis had changed considerably with the advent of antibacterial chemotherapy led us to undertake this analysis. Two recent articles[5,6] have reviewed the literature concerning this important chronic disease of childhood.

METHOD

The records of all Children's and Infant's Hospital patients with the nephrotic syndrome admitted during the period 1926 to 1948 were examined. Letters were written to the parents or physicians of patients last known to be alive but not under active treatment, asking the patients to return to the hospital for a follow-up visit. When this was not possible, the parents and physicians were asked to describe the health status of the children and to give the results of recent urine and blood pressure examinations when possible. If the child had died, the parents were asked to record the cause of death.

The analysis of the data in the records was carried out in the following manner: Charts of each case were made, showing the fluctuations in weight, proteinuria, hematuria, blood pressure and nitrogen retention over the years. These findings were correlated with the occurrence of infections and various therapeutic procedures. Criteria for a favorable prognosis were established by study of the records of patients known to be living and well. The course and findings in this group were compared with the course and findings in a group of similar cases which had ended in death, and in which the diagnosis of lipoid nephrosis was made at autopsy. Several of these autopsies have been reported by Wolbach and Blackfan[7] as examples of lipoid nephrosis.

Criteria for an unfavorable prognosis were established by a study of the records of patients who died a renal failure and in whom autopsy showed definite glomerulonephritis.

From the Department of Pediatrics, Harvard Medical School and The Children's Medical Center, Boston, Mass.

Supported by a grant, recommended by the Panel on Hematology, from the National Institute of Health of the United States Public Health Service, and also by a grant from the Mead Johnson Company.

Presented in abbreviated form at the Eastern Areal Meeting of the American Academy of Pediatrics, Buffalo, N.Y., April 29-30, May 1-2, 1948.

(Received for publication April 13, 1949.)

The distinguishing features of each of these groups of cases were determined by an analysis of the frequency and duration of such signs as hematuria, nitrogen retention and hypertension. A study was made of the causes of death in order to see what steps might be taken to reduce the mortality in the future. An effort was also made to determine what type of episode appeared to initiate remissions or exacerbations.

Definitions

For the purposes of this report, the following definitions are used:

1. *Acute glomerulonephritis*—an acute renal disease, with acute or abrupt onset usually following a pyogenic infection, in which hematuria alone or associated with edema, hypertension, azotemia and proteinuria are present for a short period of time, then gradually subside or subsequently progress into chronic glomerulonephritis.

TABLE I

New Cases of Nephrosis and Nephritis Admitted to Children's and Infant's Hospitals 1926–1946

	1926–1938	1939–1948	Total
Lipoid nephrosis	52	109	161
Nephrotic stage of glomerulonephritis	11	36	47
Total nephrotic syndrome	63	145	208
Acute glomerulonephritis	52	131	183
Chronic glomerulonephritis	24	34	58
Total acute and chronic	76	165	241
Total cases admitted	139	310	449

2. *Chronic glomerulonephritis*—a chronic renal disease following either acute glomerulonephritis or a pyogenic infection or developing insidiously, manifested by proteinuria, hematuria on occasion and ultimately by azotemia and elevated blood pressure. Edema may or may not be present, but is not the outstanding symptom except in those cases which are classified as the nephrotic syndrome.

3. *Nephrotic syndrome* (see first paragraph)—

a. *Chronic glomerulonephritis in the nephrotic stage*—A form of the nephrotic syndrome without known antecedent history of acute glomerulonephritis* or pyogenic infection, with persistent proteinuria and edema as the presenting signs, and with other evidences of chronic glomerulonephritis initially obscured, but ultimately becoming manifest.

b. *Lipoid nephrosis*—A form of the nephrotic syndrome manifested by edema, proteinuria, lipemia, essentially normal blood pressure and little, if any, hematuria or nitrogen retention at any time.

In some cases the true nature of the disease process becomes apparent only at autopsy; in others, by laboratory and clinical evidence developing during the course of the disease. For the purposes of analysis, patients who showed glomerular scarring at autopsy were classified as instances of the nephrotic stage of chronic glomerulonephritis regardless of the clinical diagnosis. Also for the purposes of analysis, patients who are now pursuing normal activity, but who have persistent albuminuria, hypertension or azotemia, have been classified (as lipoid nephrosis or the nephrotic stage of chronic glomerulonephritis) according to the diagnosis which was appropriate during the edematous phase of the disease.

* Since this study was initiated originally in an attempt to find out how to differentiate lipoid nephrosis from chronic glomerulonephritis, cases of the nephrotic syndrome following acute glomerulonephritis were arbitrarily excluded, since in them the distinction seemed clear. However, occasional cases of acute glomerulonephritis may progress into the nephrotic syndrome.

Results

Incidence

In the 23 year period, from 1926 to 1948, 208 children who entered the Children's and Infants' Hospital were diagnosed as having the nephrotic syndrome (Table I). Of these, 148 have been followed, 29 have returned questionnaires and 31 could not be reached for follow-up. One hundred sixty-one of the 208 patients fulfill the criteria for a diagnosis of lipoid nephrosis and 47 for the nephrotic stage of chronic glomerulonephritis. The records of 58 patients with chronic glomerulonephritis and of 183 with acute glomerulonephritis who were admitted to this hospital during the same period were used for statistical controls.

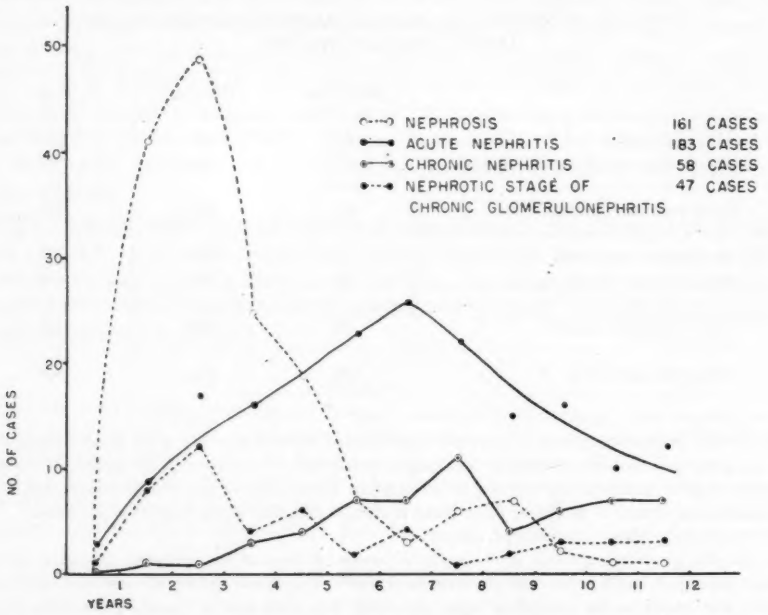


CHART 1. Age of onset of different forms of renal disease in childhood.

Age of Onset

In lipoid nephrosis, the age of onset, as shown in Chart 1, averages 3.5 years, while the average age of onset for the nephrotic stage of chronic glomerulonephritis is 4.6 years in this series. The average age of onset in the control series of children with chronic glomerulonephritis is 7.6 years, and 6.3 years in acute glomerulonephritis.*

Symptomatology and Course

Initial symptoms.—The onset in almost all instances of lipoid nephrosis and the

* In lipoid nephrosis the average age of onset is 3.5 yr. with a standard deviation of ± 2.1 yr.; in the nephrotic stage of chronic glomerulonephritis, the average is 4.6 yr. ± 3.0 yr. Since the standard error of the difference of these 2 means is 0.473, and the difference of the 2 means is 1.1 yr. or 2.3 times the standard error, the difference in age of onset of nephrosis and the nephrotic stage of glomerulonephritis is significant.

TABLE II

ONSET OF DISEASE—FIRST SYMPTOM NOTED

Symptom	Lipoid Nephrosis					Nephrotic Stage of Chronic Glomerulonephritis					Total
	Living	Dead	Lost	Total	%	Living	Dead	Lost	Total	%	
Upper respiratory infection	22	14	4	40	25	4	7	1	12	25	52
Edema of eyes	44	14	9	67	42	6	5	3	14	30	81
Wt. gain	12	14	11	37	23	6	8	0	14	30	51
Pallor	1	0	1	2	1	1	0	1	2	4	4
Generalized rash	3	1	1	5	3	1	0	0	1	2	6
Enuresis	0	1	0	1	1	0	0	0	0	0	1
Diarrhea	2	0	0	2	1	0	0	0	0	0	2
Other	6	1	0	7	4	2	2	0	4	9	11
Total	90	45	26	161		20	22	5	47		208

nephrotic stage of nephritis was insidious. The first symptoms noted were either edema around the eyes (81 cases), rapid increase in weight (51 cases) or an upper respiratory infection two or three days before the appearance of edema (52 cases). A breakdown of first symptoms reported is shown in Table II. The figures indicate that no statistically significant difference exists between the frequency of first symptoms in lipoid nephrosis and in the nephrotic stage of chronic glomerulonephritis.

TABLE III

SPONTANEOUS REMISSIONS

(Remissions not associated with obvious infections)

	Nephrosis			Nephrotic Stage of Chronic Glomerulonephritis			Total
	Living	Dead	Total	Living	Dead	Total	
Total patients	90	45	135	20	22	52	177
Patients with remissions: 1. Within 2 mo. of onset	52	22	74 (55%)	14	11	25 (60%)	99 (56%)
2. More than 2 mo. after onset	46	11	57 (42%)	4	7	11 (26%)	68 (38%)
Total patients having at least 1 spont. remission	64	26	90 (67%)	14	13	27 (64%)	117 (66%)
Patients having more than 1 spont. remission	38	9	47 (35%)	6	5	11 (26%)	58 (33%)
Total number of spont. remissions	125	44	169 (1.3)*	20	21	41 (1.0)*	210 (1.2)*

* Average no. of remissions per patient.

Sex incidence.—Ninety-nine of the 161 children with lipoid nephrosis were boys and 62 were girls. Twenty-nine of the 47 children with the nephrotic stage of chronic glomerulonephritis were boys and 18 were girls. There was, thus, a somewhat higher incidence of these renal diseases among males.

Remissions and exacerbations.—All cases of the nephrotic syndrome had edema. So-called spontaneous remissions are common within two months of the onset. As indicated in Table III, 74 of 135 children with lipoid nephrosis and 25 of 42 children with the nephrotic stage of chronic glomerulonephritis demonstrated this type of remission.

TABLE IV(A)

RESPONSE TO INFECTION

	Nephrosis		Nephrotic Stage of Chronic Nephritis		Total
Total patients	161		47		208
Patients with no infections recorded	45		13		58
Total patients with infections recorded	116		34		150
Total no. infections	298		85		383
	No.	%	No.	%	No.
Infections followed by remissions*	75	25	18	21	93
Infections followed by exacerbation*	146	49	44	52	190
Infections followed by no change	77	26	23	27	100

* Remission or exacerbation within 15 days of onset.

As the disease progresses, spontaneous remissions apparently occur less frequently for any individual patient. This is not indicated by Table III, however, which shows only that the remissions not related to any apparent infection occurred after two months in 68 instances among 177 followed cases.

Response to infection.—Any remission occurring within 15 days of an infection was considered a response to infection, since, in a series of 19 patients who had infections while observed in the hospital, 18 experienced a diuresis between 1 and 15 days following infection.

Remissions, exacerbations or no change in the patients' status may occur following infection, and no marked difference in this respect exists between the two groups of patients (Table IV(A)). Of 161 children with nephrosis, there were 298 instances of known infections.

Seventy-five (25%) of these infections were followed by remissions within 15 days, 146 (49%) by exacerbations and 77 (26%) by no change in status of the patient.

In the 47 children with the nephrotic stage of glomerulonephritis, there were 85 known infections; 21 were followed by remissions, 52% by exacerbations and 27% by no change.

In Table IV(B), the response to different types of infection is contrasted. It is quite apparent that upper respiratory infections are seldom followed by remissions and usually by exacerbations, whereas the rate of remission is roughly 40% after most other types

of infection. Again there is no significant difference in response between the two forms of the nephrotic syndrome. It is interesting to speculate whether fever, which is seldom high in upper respiratory infections, accounts for the more favorable response to other types of infection.

Recovery from lipoid nephrosis in this series of patients occurred after as few as one episode of edema or after as many as 16 exacerbations. Recovery occurred in several children even though there were no remissions from one episode of edema for as long as 12 months, though more frequently remissions occurred after one to two months of the edematous phase.

TABLE IV(B)

RELATION OF RESPONSE TO TYPE OF INFECTION

Type of Infection	Lipoid Nephrosis				Nephrotic Stage of Chronic Nephritis			
	Remission	Exacerbation	No Change	% Remissions	Remission	Exacerbation	No Change	% Remissions
Upper respiratory infection	16	96	49	10	2	34	6	5
Pneumococcus	23	23	10	41	3	6	3	25
Streptococcus*	8	6	3	47	5	2	4	45
Other	28	21	15	44	8	2	10	40

* Almost all β Str. hemolyticus.

Death occurred after 1 to 14 exacerbations. The edematous phase without remission persisted from 1 to 15 months prior to death. Apparently, there is no correlation between the number and duration of exacerbations and ultimate outcome.

Laboratory Findings

The incidence of hypertension, azotemia, and hematuria is indicated in Chart 2. Hypertension was considered to exist when the blood pressure determined with a cuff of appropriate size was above the blood pressure of standard pressure-age graphs; azotemia when the NPN was over 40 mg./100 cc.; and hematuria when more than one red blood cell per high power field was found in spun urinary sediment. Because nephrotic children with infections may temporarily show hematuria, hypertension or elevation of blood NPN, these signs were classified as persistent only if they were present for a period of one month or longer.

It will be seen that in differentiating between lipoid nephrosis and the nephrotic stage of chronic glomerulonephritis, persistent hypertension is evidence against nephrosis. Only one of the 161 children with lipoid nephrosis had hypertension for longer than one month while seen at this hospital, 33 had transient hypertension and 127 had no hypertension while under observation. Of the 47 children with the nephrotic stage of chronic glomerulonephritis, normal blood pressure was found in 14, transient hypertension in 12 and persistent hypertension in 21.

Azotemia was transient in 28 nephrotics, persisted longer than one month in 13 and was absent in 120, whereas it was transient in nine nephrotics in the nephrotic stage, persistent in 22 and absent in 16.

Persistent hematuria was found in 41 children with lipoid nephrosis, transient hema-

turia in 43 and no hematuria in 77. Gross hematuria was noted in five of these patients who are living, one of whom is well and four of whom now have albuminuria as the sole abnormal finding; in four who died, and in four who have been lost from our records. Twenty-four children in the nephrotic stage of glomerulonephritis had persistent hematuria, 10 had transient hematuria and in 13 no hematuria was noted. Gross hematuria was noted in one child who is living, in two who are no longer in our records and in four who have died. Thus hematuria has been the least helpful sign in differentiating between these two diseases, though gross hematuria is rare in lipoid nephrosis. This is

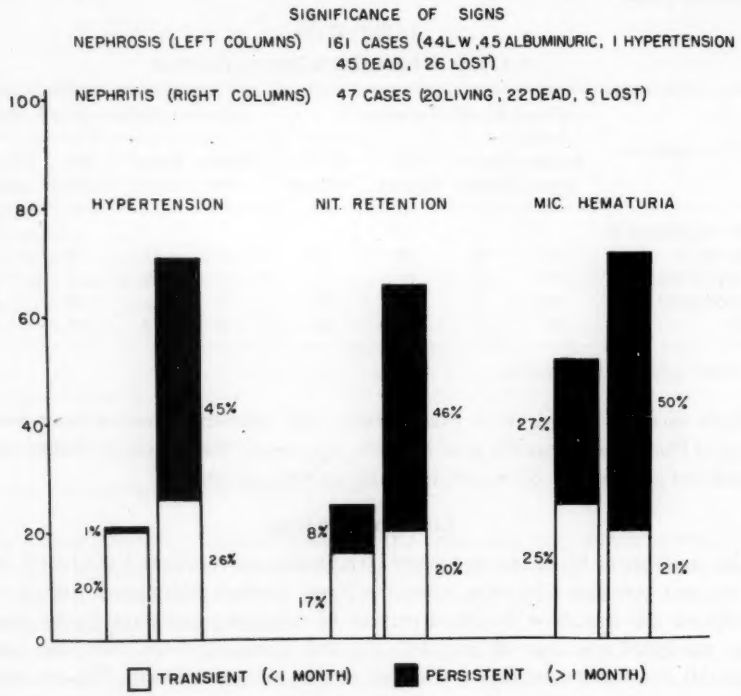


CHART 2. Diagnostic significance of major signs of renal disease.

at variance with the experience of most other students of the disease and may be explained in part by our arbitrary exclusion of cases beginning as acute glomerulonephritis from the group of cases of chronic glomerulonephritis in the nephrotic stage.

Serum cholesterol varied from 170 to 1,300 mg./100 cc. in lipoid nephrosis with more than 275 mg./100 cc. in 79 out of 88 cases in which the cholesterol was reported. Cholesterol in 19 cases of glomerulonephritis in the nephrotic stage varied from 204 to 700 mg./100 cc., with more than 275 mg./100 cc. in 16 of these 19. In several children of both groups, cholesterol was below 275 mg./100 cc. when first measured, but rose above this level one to three months after the onset of the disease.

Values for the serum protein in the children with lipoid nephrosis ranged from 2.1 to 7.4 gm./100 cc. and were less than 4.5 gm./100 cc. in 119 of 153 patients in whom measurements were made. In children in the nephrotic stage of chronic nephritis, the

serum protein ranged from 3.5 to 7.2 gm./100 cc. with 23 of 44 patients showing levels below 4.5 gm./100 cc. Of 197 patients in whom serum protein levels were reported, edema was present in 186 when the serum protein was below 4.5 gm./100 cc., and was absent when above this level. However, in nine nephrotics and seven nephritics edema was present at levels of 5 to 6 gm./100 cc. and in three nephrotics and three nephritics edema was absent at levels of 3 to 4 gm./100 cc.

Previous History

There was no constant finding of any previous disease in either group of children. Approximately one half of each group of children had been breast fed and the remainder artificially fed. About three fourths had received adequate supplements of vitamins A and D, and approximately one fourth had received none. Twenty of the children are reported to have had frequent colds. Fifteen had had tonsillectomies before the onset of nephrosis. In general, however, except for the usual childhood diseases, the children had been in good health prior to the onset of nephrosis or chronic glomerulonephritis.

Family History

An attempt was made to find a common hereditary background in these children.

A family history of allergy was found in 43 of the 161 nephrotics, and in 16 of the 47 chronic glomerulonephritics in the nephrotic stage. The significance of these figures is difficult to determine due to the varying estimates of allergy in the general population.

A family history of renal disease was found in 23 patients, of tuberculosis in 20 and of diabetes in 23 of the 206 patients.

Treatment

Table V lists 64 methods of treatment which have been used for the 208 patients while under observation in the hospital. The large number of methods of treatment indicates that few have been good enough to withstand the test of time; undoubtedly many have not been evaluated carefully.

Diet.—Seven variations in diet have been used, but none has proved therapeutically striking. We now favor a high protein low-salt diet with less than 0.5 gm. sodium chloride per day, but this is impossible to achieve, unless the child will drink salt-free milk.* Mixed vitamins are given empirically during the edematous phase.

Removal of focus of infection.—Fourteen of the 208 edematous children had otitis media requiring myringotomy. Eleven had cellulitis requiring drainage. Two had carious teeth extracted. One mastoidectomy, one rib resection for empyema, one antrotomy for sinusitis, and one pelvic abscess drainage were performed. Seventeen tonsillectomies and adenoidectomies were carried out. This has not been a routine procedure and has been performed only when the customary indications exist. When a tonsillectomy is necessary, an attempt is made to perform the operation when edema is minimal. The anesthesia department of this hospital recommends cyclopropane as the anesthetic of choice in the presence of renal damage.

Diuretics.—No diuretic has been found consistent in action. Mercurial diuretics have

* Lonalac (sodium-free milk) (Mead Johnson). It has proved useful, if the child can be induced to substitute it for ordinary milk. With Lonalac, salt-free bread and salt-free butter, an intake of 0.5 gm. sodium chloride per day can be achieved, which is still more salt than is excreted by many nephrotic children.

TABLE V

DRUGS AND PROCEDURES USED IN TREATMENT OF NEPHROSIS IN CHILDREN'S AND INFANTS' HOSPITALS, 1926–1948

Diet

- High protein low salt
- High protein
- Low salt
- Low protein
- Low fat
- Limited fluids
- Forced fluids

Removal of Infection

- Tonsillectomy and adenoidectomy
- Carious teeth removed
- Mastoidectomy
- Rib resection
- Pelvic abscess drained
- Antrotomy
- Myringotomy
- Cellulitis drained

Diuretics

- Mercupurin ®
- Salyrgan ®
- Diuretin ®
- Ammonium chloride
- Hypertonic glucose
- Hypertonic sucrose
- Aminophyllin ®
- Theophylline ®
- Theobromine ®
- Urea
- Magnesium sulfate
- Java tea
- Potassium chloride
- Potassium nitrate
- Potassium citrate
- Calcium chloride

Blood and Blood Substitutes

- Blood transfusion
- Plasma
- Concentrated serum albumin, salt-poor
- Concentrated human serum
- Immune globulin
- Acacia
- Amino acids
- Bovine serum albumin

Infections Induced

- Vaccinia
- Measles

Chemotherapeutic Drugs

- Penicillin
- Sulfadiazine
- Sulfathiazole
- Sulfapyridine
- Sulfanilamide
- Streptomycin

Other Drugs and Procedures

- Pyramidon
- Paracentesis
- Thyroid extract
- Decapsulation of kidney
- Ascorbic acid
- Testosterone propionate
- Rutin
- Vitamin A and Mazola oil
- Carbohydrate fraction of pneumococcus
- Parathormone
- Liver, intramuscular
- Horse antiserum
- Urinary antiseptics
- Digitalis
- Mixed vitamins
- Choline
- Pyridoxine
- Sweats

been used in six children. Ammonium chloride was used in six children and in no instance was there a diuresis. Hypertonic glucose and sucrose were used eight times without notable effect. Aminophyllin, theophylline and theobromine were used in five. Magnesium sulfate was given to 14 children without consistently demonstrable effect. Java tea ("Kumis kuching," an herb used chiefly in the Orient as a diuretic) was used in three children with equivocal results, although it repeatedly produced a diuresis in one child over a period of nearly a year at home. Potassium salts were given to six and calcium salts to two children.

Blood, blood derivatives and blood substitutes.—Fifty-one of the 208 children were given transfusions for anemia and as supportive therapy during infections, before the era of chemotherapy. Thirty-one children in both groups received normal human serum albumin in an attempt to initiate diuresis and increase the circulating serum albumin. Salt-poor serum albumin has produced a diuresis in approximately half the cases without increasing the serum albumin level appreciably, as reported elsewhere.[8] Six children were given human serum, four were given plasma and six were given immune serum globulin; three received amino acids, one acacia and one bovine albumin. The effects of these substances were variable.

Infections induced.—Because spontaneous diuresis frequently follows infection, especially measles, 17 children were inoculated with measles virus. Successful inoculation has been achieved by intranasal instillation of approximately 1 to 2 cc. of throat washings obtained from individuals with Koplik's spots in the oropharynx. These are collected by having the patient gargle and rinse the throat with bacteriologic broth. The washings are frozen at −70°C. until ready for use, then thawed at 37°C., and 100,000 u. each of penicillin and streptomycin are added to 2 cc. before inoculation.

This method of inoculation was used in 12 children with nephrosis and in five in the nephrotic stage of chronic glomerulonephritis. Fourteen children developed a typical macular eruption 7 to 17 days after inoculation and three failed to develop measles in spite of repeated inoculations. The children have been given chemotherapy to prevent secondary bacterial infections throughout their attack of active measles.

Of the 14 children who developed measles, 11 experienced almost complete disappearance of edema and albuminuria 1 to 12 days after onset of the rash. Three children, all chronic nephritics in the nephrotic stage, had no diuresis; two of the chronic nephritics in the nephrotic stage responded with a diuresis similarly to the nine children with nephrosis. Three of these 11 children have remained essentially edema free for two years. In the remaining eight, proteinuria and edema have recurred from one month to one year after the diuresis.[8]

Paracentesis.—Seventy-four of the 208 children required abdominal paracentesis. Of these paracentesis was performed more than one time in 43. It has been noted that paracentesis is often more effective late in the disease. One possible explanation is that early in the disease the abdominal wall is thick and edematous, and the edema fluid is spread over the body. Later in the disease, the abdominal wall is thin, edema fluid collects more easily in the abdominal cavity than in other parts of the body, and consequently is more readily released by paracentesis.

Other drugs and procedures.—Desiccated thyroid gland was given in the hospital to 11 children; several others received it at home. Even though these children apparently tolerate thyroid gland administration well, its use has been abandoned because of lack of beneficial results. Digitalis was used in five children without apparent effect. The other measures listed in the last section of Table V have been tried only one time and, because no striking improvement was noted, were discontinued. The use of chemotherapeutic drugs is discussed below.

Cause of Death

The causes of death, when the child died in the hospital, are shown in Chart 3. In the present study of 161 patients diagnosed lipoid nephrosis, 136 have been followed and, of these, 45 patients (32%) have died. Seventeen either died at home, or the cause

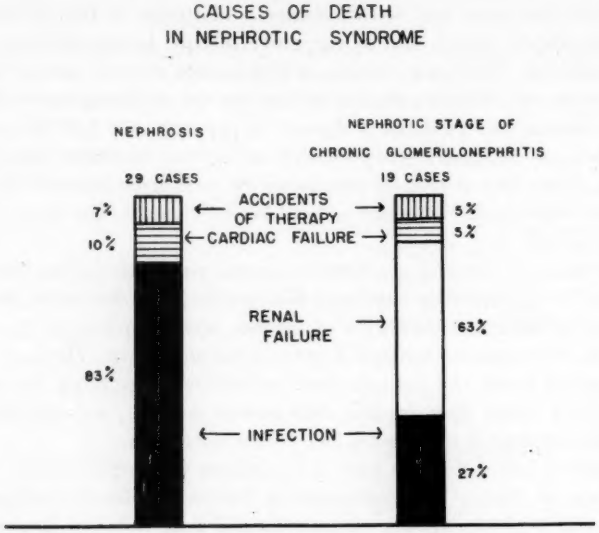


CHART 3. Comparative incidence of different causes of death in 2 forms of nephrotic syndrome. Note predominant role of infection in lipoid nephrosis.

of death was not ascertained. Of the remaining 28 patients, 23 died of infection, three of cardiac decompensation, one of anuria following sulfapyridine and one following tonsillectomy.

Twenty-two of the children in the nephrotic stage of chronic glomerulonephritis are known to have died. The cause of death has been ascertained in 19. Of these, five died of infection, one of cardiac decompensation, one of pulmonary edema following the administration of albumin and 12 in uremia.

The causes of death according to type of infection among the patients with lipoid nephrosis are shown in Chart 4. Pneumococcemia or pneumococcal peritonitis was present in 16, while the streptococcus was implicated in two and E. coli in two of the 23 cases in which infection was present at the time of death. In three cases, the organisms were not identified. It is seen that since the advent of the liberal use of sulfadiazine in 1942, few deaths have been accompanied by infection when the patient died in the hospital. Of the five hospital deaths in children with nephrosis since 1942, two were circulatory deaths, two followed infection and one death followed tonsillectomy.

One possible explanation for recent increase in the number of deaths at home may be the increase in the number of patients who have come from considerable distances. This is shown in Table VI which also indicates the higher mortality rate both before and after 1942 among children living a distance and hence presumably having less ready access to prompt medical and hospital care.

Prognosis

The prognosis of these diseases is based on the data from children followed to date. The status of these patients is briefly summarized in Tables VII and VIII. The data regarding the patients with acute and chronic glomerulonephritis in Table VII are weighted, as no special attempt was made to follow these patients after discharge from

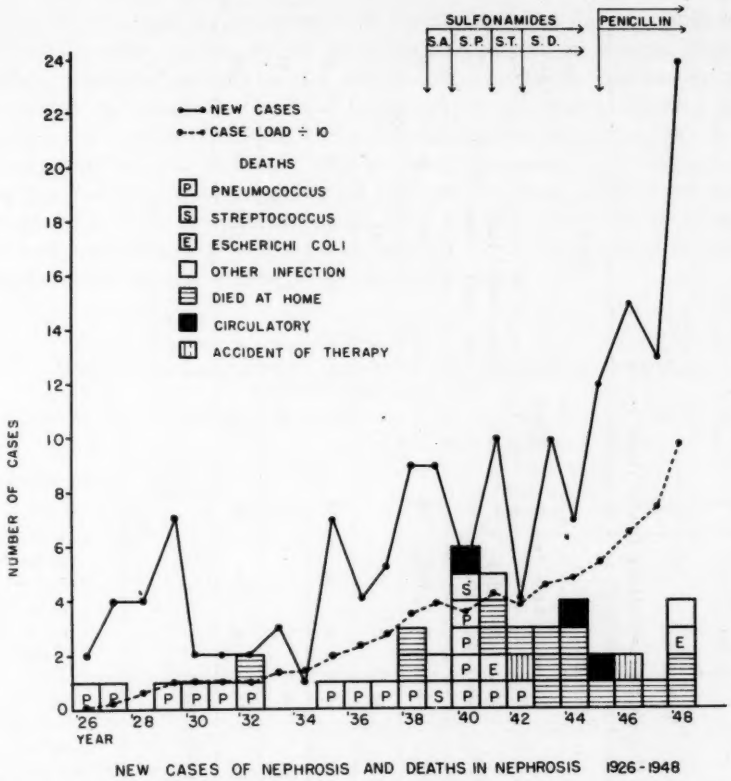


CHART 4. Causes of death in 161 cases of lipoid nephrosis with 45 deaths. Note failure of mortality to rise since introduction of sulfadiazine in 1942, despite steadily increasing case load. Also note that most deaths in recent years have occurred at home and that pneumococcus which was formerly responsible for most fatalities has not caused death since 1942.

the hospital. The criteria used for considering a patient well are freedom from edema for one year, normal blood pressure, normal serum NPN, and urine free of protein and abnormal formed elements. The children have been subdivided into three groups for purposes of analysis: those with onset before 1938—the prechemotherapy era; those with onset in the period 1939 to 1942 when sulfonamides were introduced for the treatment of infections; those with onset after 1942, when sulfadiazine began to be used for the treatment.

TABLE VI

RELATION OF DOMICILE OF PATIENTS TO MORTALITY IN 161 CASES OF LIPOID NEPHROSIS

Date of Onset	1926–1942			1943–1948		
Cases from	Total Cases	Deaths	Mortality	Total Cases	Deaths	Mortality
Greater Boston	49 (61%)	17	35%	27 (33%)	3	11%
Elsewhere	31 (39%)	15	48%	54 (67%)	10	19%

TABLE VII

CASES OF RENAL DISEASE FOLLOWED MORE THAN 2 YEARS

	Average No. Yr. Followed	Living									Dead				Total Cases
		Well				Active Renal Dis.				Total					
Year[1]		1926–1938	1939–1942	1943–1946	Total	1926–1938	1939–1942	1943–1946	Total		1926–1938	1939–1942	1943–1948	Total	
Lipoid Nephrosis	7.6	17	9	18	44	4	0	14[2]	18	62	13	16	16	45	107
Nephritis-Nephrotic Stage	6.2	0	0	0	0	2	2	3[2]	7	7	4	5	13	22	29
Chronic Nephritis[3]	5.3	0	0	0	0	0	4	4	8	8	11	6	8	25	33
Acute Nephritis[3]	5.1	19	17	17	53	9	8	8	25	78	1	2	0	3	81
Total	5.4	36	26	35	97	15	14	29	58	155	29	29	37	95	250

[1] Year for living refers to year of onset—Year for dead refers to year of death.

[2] Persistent albuminuria and edema (Onset within 4 yr.) 10
Persistent albuminuria—no edema 4
Albuminuria and hypertension 2
Hypertension—no edema 1

[3] No attempt made to recall patients to hospital.

Of 161 children with lipoid nephrosis, 45 (28%) have died. In the presulfonamide period 1926 to 1938, the average case load* was 14.6 patients per year and there were 13 deaths, a relative mortality of 6.8 patients/100/year. In the sulfonamide period 1939 to 1942, the average case load was 39 patients per year, with 16 deaths, a relative mortality of 10.3 patients/100/year. In the sulfadiazine-penicillin period 1943 to 1948, the average case load was 64 with 15 deaths, a relative mortality of 3.9/100/year.

One hundred seven children with lipoid nephrosis have been followed two or more years: 45 (42%) have died; 44 (41%) are living and well; 18 (17%) are living with evidence of renal disease. Of these latter 18, however, 10 are among the current patients, and approximately one half of these may be expected to recover.

TABLE VIII

STATUS OF 62 LIVING PATIENTS WITH LIPOID NEPHROSIS WHO HAVE BEEN FOLLOWED 2 OR MORE YEARS

Followed for	Total No. Patients	No. Patients with Major Signs				
		Proteinuria	Edema	Hypertension	Azotemia	Hematuria
16–22 yr.	9	3	0	2	0	0
11–15 yr.	9	0	0	1	0	0
6–10 yr.	12	0	0	0	0	0
4– 5 yr.	10	1	0	0	0	0
3 yr.	10	6	3	0	0	0
2 yr.	12	7	7	0	0	0

Twenty-nine children in the nephrotic stage of chronic nephritis have been followed two or more years: 22 (76%) are dead, and seven (24%) are living.

Thus, it is seen that the over-all prognosis in lipoid nephrosis before chemotherapy was favorable in approximately 40% of the cases. Since the introduction of sulfadiazine and the newer antibiotics, the mortality rate has been reduced further (from 6.8 to 3.1 patients/100/year). Presumably, in a longer follow-up, actual mortality will also be shown to be reduced. Almost all of the nephrotic children who have died since 1942 have died at home. Perhaps, had certain supportive measures, such as are available at the hospital, been used, these patients might have tolerated whatever crisis caused their death.

It remains impossible, however, to give a favorable prognosis in either chronic glomer-

* Case load is the number of living patients followed during the year plus the number of new patients for that year with evidence of active renal disease. Thirty-three chronic nephritics have been followed (76% mortality). Of 183 patients with acute glomerulonephritis, 81 have been followed longer than 2 yr. The majority of the 102 others are presumed to be well as only those with subsequent difficulty are likely to return to the hospital. Fifty-three of the 81 are known to be well, 25 have become chronic and 3 died of cardiac decompensation during the acute illness.

ulonephritis or the nephrotic syndrome of chronic glomerulonephritis, though children with the latter may live 10 years or longer with their disease.

Duration of Disease

In the series of 62 children who have been followed two or more years with recovery, the course of nephrosis has persisted from 6 to 96 months. In all but a few, active disease lasted between one and three years (2 ± 1.2 years). Of those nephrotics who died, death occurred between 2 and 95 months after onset, but usually within two years.

Growth and Development

Growth and development usually are delayed during the active phase of nephrosis, but following recovery, the patient assumes his normal growth channel as plotted on standard height-weight anthropometric charts. Only one patient has shown mental retardation. The children apparently do average school work, and no attempt has been made to do routine psychometric examinations.

Discussion

Our observations are similar to those reported by Schwarz,[1] Murphy,[2] Heyman,[3] and Block.[4] The mortality among our patients as well as the laboratory and clinical findings are comparable to those recorded in their series.

Using the criteria for differential diagnosis as outlined, the differentiation between lipoid nephrosis and the nephrotic stage of chronic glomerulonephritis has been difficult, but possible. Fourteen diagnoses among 208 cases have had to be changed, either as a result of autopsy reports or the appearance of such symptoms and signs as hematuria, hypertension or nitrogen retention. However, many patients had to be followed for a considerable time, even up to one year, before a definite distinction could be made.

Glomerular changes have been noted at autopsy in 5 of 17 patients in whom a clinical diagnosis of lipoid nephrosis had been made. However, in all of these five, tubular degeneration predominated, and in four of the five atypical signs and symptoms had been noted at some time. This is not the place to discuss whether lipoid nephrosis and the nephrotic stage of chronic glomerulonephritis are actually two different diseases or two different variants of the same fundamental pathologic process. It is clear that certain instances of the nephrotic syndrome which we classify as lipoid nephrosis have a relatively good prognosis, while those in which the features of chronic glomerulonephritis predominate have a poor prognosis. It is quite possible that in certain cases, glomerulonephritis may be superimposed on an original lipoid nephrosis, giving a mixed picture, just as pyelonephritis or vascular sclerosis may complicate other forms of renal disease.

More exact information concerning the physiologic and anatomic derangements in the nephrotic syndrome can come only from the correlation of careful studies of renal function by the newer methods with the clinical course and ultimate autopsy findings in those patients who succumb to intercurrent infection or to the disease itself. Such studies are under way in our own as well as in a number of other clinics.[9] Unfortunately, the renal function tests used in the past did not yield information which could allow one to determine whether some cases of so-called lipoid nephrosis with clinical or apparent recovery actually ended up with reduced renal function. For the purposes of this initial follow-up study, we have had to rely on ordinary clinical examination with routine urinalysis. The fact that, in the group of nine patients followed for 16 or more years, pro-

teinuria has been found in three, and hypertension in two, suggests that clinical recovery from nephrosis in childhood does not always imply complete restoration of the kidney to normal. This would be in line with Rennie's observations.[10]

Because of the difficulty in distinguishing between the two types of cases and because lipoid nephrosis appears to be relatively common in childhood, all patients with edema, lipemia, low serum proteins and albuminuria should be treated with a reasonable degree of optimism. The disease will run a chronic course with remissions and exacerbations, but ultimate recovery will occur in many children, particularly if one can protect the patient from infection, which has been the major cause of death in the past. Those patients who develop frank evidence of glomerular involvement, however, usually assume the poor prognosis of chronic nephritis.

One of our chief purposes in making this study has been to place our own therapeutic program for these patients on a sounder footing. The following comments represent our current views regarding the management of nephrosis based on this study and our present experience. It is clear that, as in so many chronic diseases of unknown etiology, the physician can do little in the way of treatment which affects the real course of the disease. On the other hand his therapeutic program should be aimed at protecting the patient so far as possible from any special hazards which he runs and at minimizing the damage caused by the disease. Since the major cause of death in patients with lipoid nephrosis is infection, every effort should be made to diminish the frequency of infection and to treat established infections promptly and thoroughly. The prevention of respiratory infections is difficult, but can be accomplished to a considerable extent by cutting down the contacts of the patient with people outside the family, particularly children during the winter months. The continuous use of sulfonamides or of antibiotics in prophylactic doses deserves investigation, but cannot be recommended until its safety and effectiveness are demonstrated under controlled conditions. Most important is education of the parents to prompt recognition of symptoms of infection, particularly fever, so that chemotherapy may be instituted promptly, thus controlling bacteremia and preventing the development of peritonitis. In view of the fact that fatal infections due to E. coli have occurred in several of our patients, combined penicillin and streptomycin therapy is probably indicated in all severe infections, at least until the organism is identified.

The second hazard which threatens the nephrotic child is the unwillingness of physicians or parents to accept the fact that the disease is apt to run its natural course regardless of what treatment is administered. The consequence of this natural reaction to any chronic disease, particularly one which so profoundly affects the appearance of the patient as nephrosis, is a continuous and valiant struggle to eliminate the edema. This results in prolonged hospitalization, which submits the patient to repeated exposures to infectious agents, and leads to considerable unnecessary emotional trauma for both child and parents. In addition to these subtle but important detrimental effects, the patient is plied with diuretics, with intravenous infusions of all sorts, and, if any foci of infection are found, these are removed. The diuretics, certainly the mercurials, may in themselves damage the kidney, intravenous infusions of concentrated plasma or even serum albumin may be ineffective or may precipitate pulmonary edema if large doses are given to a child with hypertension, and the removal of foci, such as the tonsils and adenoids, may be dangerous during the edematous phase. We believe in keeping patients at home or in a sheltered environment as much as possible.

There is no known reason why a child with nephrosis should not be ambulatory as

long as the edema permits activity. The diet should be as low in sodium as possible, provided an adequate caloric intake, with a considerable amount of protein, can be maintained. Paracentesis remains the simplest method of removing extracellular fluid in those children who have considerable ascites, and in whom the accumulation of fluid becomes so great as to embarrass eating, breathing or getting about.

Better methods of treatment will have to await a clearer understanding of the nature of the disease process. Serum albumin may be useful in relieving edema in some patients, but, because of its rapid excretion in the urine, its effect is apt to be transitory. Moreover, more data upon its effects on renal function are needed, before one can be absolutely sure that it is not injurious to the nephrotic kidney. The value of measles inoculation as a therapeutic measure is not clear as yet, although it produces striking remissions in many, but not all patients.

Few diseases tax the resources of the practitioner so extensively as the nephrotic syndrome. He must be a combination of infectious disease expert, nutritionist, physiologist and psychiatrist for the patient and, above all, guide, counsellor and friend to the parents, who have to live, day in and day out, for two or three years with a child who eats poorly and often has periods of irritability or depression, who frequently vomits or has diarrhea, whose appearance may become grotesque at times, and who may become desperately sick with peritonitis and bacteremia at any moment. On the other hand, the satisfaction of seeing a patient restored to normal health and activity after several years of nephrotic edema is well worth the time and patience required.

Conclusions

The records of 208 patients with the nephrotic syndrome seen in the Children's and Infants' Hospitals of Boston from 1926 to 1948 have been reviewed.

The main criteria found for differentiating between lipoid nephrosis and the nephrotic stage of chronic glomerulonephritis have been the presence of hypertension or azotemia for longer than one month in patients with the latter disease, which occurs more frequently in children over four years of age. Other features of the two diseases may be indistinguishable. Nonetheless, it is desirable to differentiate between them, as apparently few if any patients recover from the nephrotic syndrome if the evidences of glomerulonephritis are clear-cut.

Lipoid nephrosis is characterized by the insidious onset of edema in young children, usually between the ages of one and four. Findings include edema, hypoproteinemia, hypercholesterolemia and heavy proteinuria. Blood pressure may be elevated for short periods, but rarely over one month. Microscopic hematuria does not exclude the diagnosis, though macroscopic hematuria is usually evidence of glomerular involvement.

Symptoms and findings in lipoid nephrosis may persist for from one to three years without specific therapy. Exacerbations with infection, followed by remissions shortly after the infection, and remission soon after the onset of the disease are relatively common. Prognosis is not related to the number or duration of exacerbations. Death before 1942 was chiefly due to an intercurrent infection. Since 1942, with the advent of sulfadiazine and the newer antibiotics, death from infection has become less common, and has usually occurred at home, presumably because treatment was not promptly instituted.

There is apparently no constitutional defect in these children before the onset of the disease, and growth and development are normal after recovery.

No form of treatment has been found wholly satisfactory. Paracentesis, transfusion and

low salt diet are the most common supportive measures used here. Antibiotics are valuable during infections and have apparently lowered the mortality of the disease in recent years. Focal sources of infection should be eliminated by operative procedure only when surgical intervention is definitely indicated. Injections of salt-poor concentrated human serum albumin and the induction of measles are being evaluated as methods of inducing a diuresis.

In this series approximately one half of the patients with a clinical diagnosis of lipoid nephrosis have apparently recovered completely without residual disease, while a small number show persistent albuminuria or hypertension. It is hoped that with closer supervision of the patients and with adequate chemotherapy, this figure can be significantly increased in the future.

ACKNOWLEDGMENT

The authors wish to thank Miss Jane Worcester, A.B., M.D., S.D., of the Department of Biostatistics of the Harvard School of Public Health, for her guidance in the analysis and preparation of tables.

REFERENCES

1. Schwartz, H., Kohn., J., and Weiner, S., Lipoid nephrosis: Observations over period of 20 years, Am. J. Dis. Child. **65**:355, 1943.
2. Murphy, F. D., Warfield, L. M., Grill, J., and Annis, E., Lipoid nephrosis: Study of 9 patients, with special reference to those observed over long period, Arch. Int. Med. **62**:355, 1938.
3. Heyman, W., and Startzman, V., Lipemic nephrosis, J. Pediat. **28**:177, 1946.
4. Block, W. M., Jackson, R. L., Stearns, G., and Butsch, M. P., Lipoid nephrosis: Clinical and biochemical studies of 40 children, 10 with necropsies, PEDIATRICS **1**:733, 1948.
5. Bradley, S. E., and Tyson, C. J., Nephrotic syndrome, New England J. Med. **238**:233 and 260, 1948.
6. Farr, L. E., Nephrosis, Advances in Int. Med. **1**:225, 1942.
7. Wolbach, S. B., and Blackfan, K. D., Clinical and pathological studies on so-called tubular nephritis (nephrosis), Am. J. M. Sc. **180**:453, 1930.
8. Janeway, C. A., and others, Diuresis in children with nephrosis: Comparison of response to injection of normal human serum albumin and to infection, particularly measles, Tr. A. Am. Physicians **61**:108, 1948.
9. Galan, E., Nephrosis in children, Am. J. Dis. Child. **77**:328, 1949.
10. Rennie, J. B., Oedematous syndrome of nephritis with special reference to prognosis, Quart. J. Med. **16**:21, 1947.

SPANISH ABSTRACT

Síndroma Nefrótico
I. Historia Natural de la Enfermedad

Se han revisado los records de 208 pacientes con síndroma nefrótico vistos desde 1926 hasta 1948. Los criterios principales que se han encontrado para diferenciar entre la nefrosis lipoide y la etapa nefrótica de glomerulonefritis crónica han sido la presencia de hipertensión y azotemia por más de un mes en pacientes con esta última enfermedad.

La nefrosis lipoide se caracteriza por el principio insidioso de edema en niños pequeños, generalmente entre las edades de 1 y 4 años. Los descubrimientos incluyen edema, hipoproteinemia, hipercolesterolemia y fuerte proteinuria. Los síntomas y los descubrimientos en nefrosis lipoide generalmente persisten de 1 a 3 años sin terapia específica. El prognóstico no se relaciona con el número de remisiones y exacerbaciones y ha mejorado con el advenimiento de la sulfadiazina y antibióticos más nuevos, ya que la infección es responsable por la mayor parte de las muertes.

Por otra parte, en la etapa nefrótica de glomerulonefritis crónica el prognóstico es todavía pobre y el desorden renal es la causa principal de muerte.

300 Longwood Avenue

Pediatrics

VOLUME 5 MARCH 1950 NUMBER 3

AMERICAN ACADEMY OF PEDIATRICS, INC. PROCEEDINGS AND REPORTS

MEETING OF THE STATE CHAIRMEN

San Francisco, Calif.—November 13, 1949

The meeting was called to order by Dr. Warren R. Sisson on Sunday, Nov. 13, 1949, at 1:45 p.m. Dr. Edward B. Shaw, President-Elect, presided during the rest of the session.

The first order of business was the discussion of the report of the Committee on Reorganization. After a preliminary statement by Dr. Borden S. Veeder, explaining many of the details, the report was presented by Dr. James M. Baty. After considerable discussion of various points, the Chairmen voted to concur in the action taken by the Executive Board in approving this report, the report to be submitted to the members for mail vote.

The next order of business was the question of State Chairmen. The following proposed amendment to the By-Laws was presented as coming from the Executive Board: "That each state be represented by one State Chairman; that State Chairman may designate as many Alternate State Chairmen to assist him as he finds desirable but only one would act as the representative for each state." The group from New York objected to this change and, after discussion, the matter was remanded to the Executive Board meeting in June for decision.

Dr. Edgar E. Martmer read a letter from Dr. William Black and a proposition from Dr. John K. Glen. The State Chairmen voted that they were not in favor of Dr. Black's letter, but that they would approve of Dr. Glen's suggestion that the Committee on Legislation, where possible, communicate with the membership before taking final action on any national legislation.

Dr. Clarence E. Webb of Louisiana brought up the question of the Southern Medical meetings, which was acute this year, and Dr. Martmer explained that the Academy was largely governed by the availability of hotel facilities; that in 1950 and 1951 the meetings would be in October. In this way, they would not conflict with the Southern Medical meetings.

After some discussion, the meeting adjourned at 4:15 p.m.

REPORT OF THE EXECUTIVE BOARD MEETING

San Francisco, Calif.—November 11, 12, 13 and 15, 1949

A meeting of the Executive Board of the American Academy of Pediatrics was held at the Palace Hotel, San Francisco, Calif., on Friday, Nov. 11, 1949. It was called to order at 10:00 a.m. by the President, Dr. Warren R. Sisson. There were present Drs. Sisson, Shaw, Barba, Beaven, Bost, London, Munns, McElhenney, Stringfield, Wishropp, Grulee, Martmer, Pease and Bakwin.

The first order of business was the consideration of applicants: the following were approved.

District I

Dr. Benjamin Wells Bullen, Jr., Greenwich, Conn.
Dr. William Anderson Dickson, Boston, Mass.
Dr. Theodore S. Golden, Framingham, Mass.
Dr. Maurice J. Keller, Salem, Mass.
Dr. Henry M. Putnam, Dedham, Mass.
Dr. Benjamin Reder, Fall River, Mass.
Dr. James Harold Root, Jr., Waterbury, Conn.
Dr. Martin Rothman, Haverhill, Mass.

Affiliates in Surgery

Dr. Henry Hudson, Jr., Brookline, Mass.
Dr. Dudley Ross, Montreal, Quebec, Canada

District II

Dr. Edgar L. Clayton, Hicksville, N.Y.
Dr. Joseph H. Fries, Brooklyn, N.Y.
Dr. Seymour Gruber, Brooklyn, N.Y.
Dr. Isaac William Karlin, Brooklyn, N.Y.
Dr. Martha L. Smith, New York, N.Y.
Dr. Edward H. Townsend, Jr., Rochester, N.Y.
Dr. Robert Warner, Buffalo, N.Y.

Reinstatement

Dr. Henry N. Pratt, New York, N.Y.

Affiliates in Surgery

Dr. Ernest E. Arnheim, New York, N.Y.
Dr. Elliott S. Hurwitt, New York, N.Y.
Dr. Robert R. White, Rochester, N.Y.

District III

Dr. Benjamin Dickstein, Philadelphia, Pa.
Dr. Matthew Feldman, River Edge, N.J.
Dr. Theodore M. Ginsburg, Philadelphia, Pa.
Dr. William Burton Greenberg, West New York, N.J.
Dr. Paul Brooks Kreitz, Bethlehem, Pa.
Dr. Frank Strattan White, Teaneck, N.J.

District IV

Dr. Edward Davens, Mt. Washington, Md.
Dr. Gene B. Haber, Hyattsville, Md.
Dr. Warren D. Leslie, Wheeling, W.Va.
Dr. James Neill Lysaught, Baltimore, Md.
Dr. John Oliver Nestor, Arlington, Va.
Dr. Francis F. Schwentker, Baltimore, Md.
Dr. Arthur I. Sims, Arlington, Va.
Dr. George Roland Spence, Silver Spring, Md.
Dr. Melchijah Spragins, Towson, Baltimore, Md.
Dr. Mack Sutton, Albany, Ga.
Dr. Helen B. Taussig, Baltimore, Md.
Dr. Elizabeth Peabody Trevett, Annapolis, Md.

District V

Dr. Edward A. Sawan, Akron, Ohio
Dr. Harold C. Epstein, Cleveland, Ohio

Dr. Zolton Leb Klein, Cleveland, Ohio
Dr. Lillian Marks, Columbus, Ohio
Dr. Louise W. Rauh, Cincinnati, Ohio
Dr. William Thronton Mustard, Toronto, Ontario, Canada

District VI

Dr. Joshua E. Bacon, Dubuque, Iowa
Dr. Howard L. Lange, Belleville, Ill.
Dr. C. Richard Yoder, Bloomington, Ill.

District VII

Dr. Mary Clark, Hattiesburg, Miss.
Dr. Samuel Chester Dunn, Kingsville, Texas
Dr. Martha Helen Hale, Dallas, Texas
Dr. Byron Arthur Jenkins, Lubbock, Texas

District VIII

Dr. Charles Macfie Campbell, Jr., Santa Barbara, Calif.
Dr. Louis T. Campbell, Eugene, Ore.
Dr. Cornelius S. Meeker, Butte, Mont.
Dr. Belle Dale Poole, Pasadena, Calif.

Reinstatement

Dr. Arthur H. Hurd, Pasadena, Calif.

District IX

Argentina

Dr. Alfonso Alberto Bonduel, Buenos Aires
Dr. Juan R. Diaz Nielsen, Buenos Aires
Dr. José Maria Albores, Buenos Aires
Dr. Raúl Maggi, Buenos Aires
Dr. Rafael R. L. Sampayo, Buenos Aires
Dr. Arturo Manuel de San Martin, Buenos Aires

Brasil

Dr. Wiberto Guedes Pereira, Rio de Janeiro

Chile

Dr. Pedro Araya Chiappa, Santiago
Dr. Ricardo Olea Guldemont, Santiago
Dr. Osvaldo Montes Rodríguez, Santiago
Dr. Gaston Duffau Ortiz, Santiago
Dr. Raul Gantes Arestizábal, Santiago
Dr. Alfredo Widerhold Rotter, Santiago

Cuba

Dr. Alberto C. Mata Lavin, Habana

The following requests for Emeritus Fellowship were approved:

Dr. Gregorio Araoz Alfaro, Buenos Aires, Argentina
Dr. A. W. Chapman, Glens Falls, N.Y.
Dr. Joseph Garland, Boston, Mass.
Dr. W. Morgan Hartshorn, New York, N.Y.
Dr. William W. Howell, Jamaica Plain, Mass.
Dr. C. Carroll Jones, Bloomington, Ill.
Dr. Newell L. Moore, Santa Ana, Calif.
Dr. Louis S. Robins, Chicago, Ill.
Dr. O. N. Torian, Sewanee, Tenn.

Dr. John Zahorsky, Steelville, Mo.
Dr. William Falkener, Newport News, Va.

The following resignations were accepted:

Dr. Pedro Cantonnet, Montevideo, Uruguay
Dr. R. R. Struthers, Paris, France

The request of Dr. Amelia Burns Sheftall, Jacksonville, Fla., for a leave of absence was granted for 2 years, effective June 30, 1949.

The request of Dr. Gerti Dooneief, Bedford Hills, N.Y., for an extension of leave of absence was granted for 1 year to June 30, 1950.

Dr. William M. Happ, Escondido, Calif., was transferred from Emeritus Fellowship to Fellowship.

President's Report

This gives me an opportunity to speak briefly of the Executive Board meetings. They offer the greatest opportunity for considered opinion and guidance of Academy affairs that exists in our organization. As your President, I have been greatly impressed by the good balance of the membership, its great sense of responsibility to the Academy and its untiring efforts. I feel that the deliberations or minutes of the Executive Board should be distributed to the members as early as possible while interest still exists in current discussions. One cannot overemphasize the importance of putting the deliberations of the Board out in an attractive format to encourage greater publicity. In spite of my New England streak of economy, I would earnestly recommend quarterly meetings of the Board and placing more emphasis upon the policies of the Academy in planning our activities in the broad field of public health. I do not see how this can be done without frequent meetings and assignment of special subjects to special committees of the governing body. In this connection I recommend that the Executive Board be thoroughly conversant with the finances of the Academy and appoint the Budget Committee from its membership.

The second subject which I would like to bring to your attention is that of public relations. Early in my term of office, you voted to appoint a committee to investigate this subject. It has seemed to your President one of the important activities of the Academy. It has been a widespread criticism of the members that they were uninformed in regard to the activities of the Academy. Your committee has given this subject careful study and I hope you will act favorably upon its report. From my experience as your President, I would like to append the thought that funds spent wisely for public relations and publicity will greatly enhance the position of the Academy, its individual members and the health of children. I am pleased to report that especially through the efforts of individual members of the Executive Board there has taken place great improvement in our public relations with the American Medical Association. A liaison committee from each organization has been established and this committee, through its chairman, Dr. Philip S. Barba, has developed excellent rapport. We know the officers and trustees of the American Medical Association and they know us. I can report unhesitatingly that one can be optimistic in regard to excellent cooperation between these groups of organized medicine. My report on this subject would be incomplete without mentioning the name of Dr. Oliver L. Stringfield, for by his unselfish efforts and tact much has been accomplished.

Closely associated with the subject of public relations is the dinner given this spring at the Hotel Roosevelt, announcing the publication of our Study of Child Health Services by the Commonwealth Fund. This undoubtedly represented the pinnacle of Academy achievements, as evidenced by the acknowledgment by the press. It is fitting to mention the names of Dr Stringfield, Dr. Barba, Dr. Hubbard and Mr. Hiller, who made possible this memorable occasion. I am pleased to report that the Study publications on both a national and state level have met with great enthusiasm by all interested in better distribution of health services to children. The fact that the Lasker Award was given to the Academy is further evidence of our contribution in stimulating better health for children.

You will recall that in April of this year in Atlanta, Ga., a special meeting of the Executive Board was called by your President. The occasion was the need for a reorganization of the executive structure of the Academy. The ship was carrying more than the legal cargo. The ICH Committee, a most important part of the Academy, was becoming an overgrown child with adolescent problems and very expensive to educate. The main offices in Evanston were overworked by the great increase in the business affairs and routine management of the Academy. The Secretary had less and less time for the problems that lay outside his office and related to national and state pediatric interests. Overlapping of the activities of the Secretary and the Director of the ICH Committee seemed inevitable. I am

pleased to report that the committee you appointed to submit a new plan has held repeated meetings and after reviews by the State Chairmen has a proposal for your consideration. It is my belief that the majority of the members think that reorganization is urgent.

The essential plan recommends consolidation of activities in one office, disbanding of the ICH Committee, and the creation of a new officer called "Executive Secretary" who would have the over-all supervision of the Academy under the Executive Board. The plan calls for a new committee which will retain interest in the area of public health, plan and advise and suggest committees which will stimulate action in this field, and work effectively with other agencies interested in child health at national, state and local levels. You have been briefed in the details of the proposal and your decisions at this meeting will determine the Academy's future development and place in American medicine.

Finally, a word concerning the ICH Committee. In my opinion, it has laid the ground work for a new and expanding Academy. It has presented an interpretative report and recommendations for your consideration. It is essential to remember that this committee has worked with rather indefinite directives from the Executive Board, has raised most of the funds for its activities, and has gradually assumed some of the responsibilities which must be incorporated in our central organization. In the interim before the reorganization takes place, it seems most desirable to retain the valuable experience of this committee, holding our place in the field of child health. This necessitates financial support from the Academy for a short period of time and this matter must be given most careful consideration. It would seem to me an error in judgment to interrupt at this time the plan for this committee as outlined in Dr. Hill's report of 2 years ago. In my opinion, the Academy has reached its greatest influence in child health and the interest of the members was never greater.

The accomplishments of the Academy reflect in no small degree the leadership of its past Presidents and the high idealism and devotion of its Secretary and Treasurer, Dr. Grulee. I have complete faith in the future of our organization.

Respectfully submitted,

WARREN R. SISSON, *President*

The Secretary's Report was presented as follows:

For the period since the last meeting of the Executive Board in June, the activities of the Academy have been taken up largely with the work of the Reorganization Committee and the situation as regards the ICH Committee. The two are so intimately connected that it is not possible to separate them. It became evident at the meeting in June that the ICH Committee could not proceed in the manner in which it had previously, because of lack of funds.* This had become evident to other members of the Executive Board and especially the President. As a consequence of this, there had been called in April a meeting of the Executive Board for the purpose of considering the advisability of appointing a Reorganization Committee in place of the one which already existed. Unfortunately, the Secretary was ill at the time of this meeting and could not be present. There is, apparently, a great deal of difference of opinion as to where the stress should be laid with respect to the activities of the Academy. Apparently, everyone feels that all the branches of the Academy should be combined into one area and that we should not have two or three offices because it is not economically wise. The first question is how they should be organized and what should be done about committees, especially the ICH Committee. These are matters to be taken up at the meetings of the Executive Board, State Chairmen and of the Academy in its business meeting.

The pamphlet, "Standards and Recommendations for Hospital Care of Newborn Infants—Full-Term and Premature," under the jurisdiction of the Committee on Fetus and Newborn, is selling regularly and we have had to add to the initial supply. However, there are plenty of pamphlets on hand and they can be obtained through the Central Office.

A revision of the pamphlet, "Report of the Committee on Therapeutic Procedures for Acute Infectious Diseases and on Biologicals of the American Academy of Pediatrics," is in the process of preparation now and should be out before long.

Of the various committee groups, the ICH Committee, of course, has been quite active in various fields, of which you have been apprised.

---

* Recently, Dr. Beaven has been able to obtain a grant of $2500 from the Albert H. and Jessie D. Wiggin Foundation and the Connecticut group has repaid $1000 to the Academy, which had been loaned to them for the completion of their State Survey. It may be that this latter fund will be contributed by the Board to the ICH Committee; certainly the former was so intended.

Although the Committee on Cooperation with the American Legion, under the leadership of Dr. James G. Hughes, has had many disappointments after many years of conferring with the American Legion on health topics for children, it is altogether likely that they will obtain some definite results in the near future.

The Committee on School Health, under the Chairmanship of Dr. Thomas Shaffer, has also been active and has had several conferences of value.

The Committee on Legislation has, as usual, kept in close contact with the situation in Washington and has kept the Executive Board in touch with legislation.

The Committee on Care of European Children has continued its activities and we should be proud of the work it is doing.

The Committee on Tumor Registry has become quite active and has recently received a grant from the Babe Ruth Cancer Fund. This will be a great help to the Committee.

The Publication Committee, of which Dr. Frank H. Lancaster is Chairman, has been most active in determining the finances of PEDIATRICS and has been most helpful in advice as to future conduct of that journal. Needless to say, Dr. Hugh McCulloch and his Editorial Board, which has recently been increased by the appointments of Dr. L. Emmett Holt, Jr., Dr. Herbert C. Miller and Dr. Ralph Platou, have worked most efficiently and we may be very proud of the results of their efforts.

The difficulties with the Latin American group are principally financial. Many of them are forced to give up their membership in the Academy, not because of lack of interest, but because the exchange situation is so serious that it is almost impossible to get American dollars to pay their dues.

The Pan-American Congress, which occurs every third year, has just been completed at Mexico City.

The Section on Surgery is already in good working order. The Affiliates in Surgery are increasing in number under the guidance of Dr. Herbert E. Coe, and Dr. Bret Ratner has about completed his plans for the Affiliates in Allergy.

Dr. Milton J. E. Senn is still working on plans for the Affiliates in Psychology and Psychiatry but it looks as if we would have these all in definite shape in the near future.

It was thought necessary by the President to have a special committee to act with the AMA. Dr. Philip S. Barba was named Chairman. This Committee has been quite active and has met with a cordial reception by the Board of Trustees of the AMA.

For some time, the Executive Board has felt the need for publicity and public relations. There is a Committee, under the Chairmanship of Dr. Barba, working along these lines. It will be remembered that we had such a connection and that recently, until the resignation of Mr. Hiller, the ICH Committee had such representation. It is felt that we should have some means of working on our external relations other than our own efforts and that we need both cooperation and guidance.

Dr. Oliver L. Stringfield and Dr. Rustin McIntosh have been named representatives of the Academy on the American Committee of the Sixth International Congress of Pediatrics to be held in Zurich, Switzerland, July 24 to July 28, 1950.

It is my unfortunate duty to present the names of those who have died since my last report: Charles A. Aldrich, Rochester, Minn.; Catherine S. Amatruda, New Haven, Conn.; John William Amesse (Emeritus), Denver, Colo.; Katharine Baird, Wauwatosa, Wis.; Paul E. Belknap, Topeka, Kan.; Jose Bonaba, Montevideo, Uruguay; Charles J. Cole, Philadelphia, Pa.; Thomas J. Donovan, Houston, Texas, Pedro de Elizalde, Buenos Aires, Argentina; Kurt H. Falkenheim, Rochester, N.Y.; George C. Glass, Hartford, Conn.; Hal R. Hoobler, Oakland, Calif.; George D. Lyman, San Francisco, Calif.; Stanley Nichols, Long Branch, N.J.; Louis Simonson, Newark, N.J., and Henry W. Titus, New Rochelle, N.Y.

Deaths which have occurred since the Atlantic City, N.J., meeting—to be reported at the San Francisco Business Meeting: George L. Cook, Tampa, Fla.; R. S. Friedley (Emeritus), Akron, Ohio; Elmer G. Horton (Emeritus), Columbus, Ohio; Abraham M. Litvak, Brooklyn, N.Y.; John Lyttle, Los Angeles, Calif.; James H. McKee (Emeritus), Philadelphia, Pa.; Martin G. Neeley, Birmingham, Ala.; Worth Ross, Hartford, Conn.; Eugene Rush, Philadelphia, Pa.; M. Scherzer, Montreal, Canada; Lilliam R. Smith, Hardwich, Mass.; Silas S. Snider, Chicago, Ill.; Frederick F. Tisdall, Toronto, Ontario, Canada.

Respectfully submitted,

CLIFFORD G. GRULEE, *Secretary*

The Secretary's Report was accepted.

The Treasurer's Report was presented as follows:

STATEMENT OF RECEIPTS AND DISBURSEMENTS
JULY 1, 1949, to SEPT. 30, 1949

Balance in checking a/c—July 1, 1949			$ 54,197.32
Balance in savings a/c—State Bank & Trust Company			24,252.31
Balance in savings a/c—First National Bank & Trust Co.			9,268.49
			$ 87,718.12
Receipts			
Dues		$ 58,887.67	
Exhibits—San Francisco, Calif., Nov. 1949		7,925.00	
Annual Meeting—San Francisco—Seminars		850.00	
Registration		3,238.00	
Round Tables		1,644.00	
Initiation Fees		1,500.00	
Interest Earned		327.50	
Committee—Improvement of Child Health		3,500.00	
Special Fund for Child Care (Connecticut)		1,000.00	
Pamphlets—Child Health Records	$ 93.75		
Immunization Procedures	69.04		
Newborn Manual	261.66	424.45	
Certificate		1.00	
PEDIATRICS		20,518.00	99,815.62
			$187,533.74
Disbursements			
Annual Meeting—San Francisco, Calif.		822.04	
Areal Meeting—Philadelphia, Pa.		100.75	
Bank Charge and Exchange		36.98	
Executive Board		1,738.18	
Miscellaneous		256.35	
Office Supplies and Equipment		290.97	
PEDIATRICS		20,518.00	
Postage		281.53	
Rent		681.61	
Salaries—Secretary	$ 4,500.00		
Ass't Secretary	1,249.99		
Office	2,884.11	8,634.10	
Stationery and Printing		274.97	
Telephone and Telegraph		160.09	
Travel Secretary		105.34	
Treasurer's Bonds		82.50	
Expense—Districts	17.51		
States	58.75		
Committees	13,721.50	13,797.76	
Pamphlets—Child Health Records	17.13		
Immunization Procedures	3.64		
Newborn Manual	878.39	899.16	48,680.33
Balance—Sept. 30, 1949			$138,853.41
Balance in checking a/c—Sept. 30, 1949			89,634.38
Balance in savings a/c—State Bank & Trust Co.			25,752.31
Balance in savings a/c—First National Bank & Trust Co.			23,466.72
			$138,853.41

The Treasurer's Report was accepted.

FINANCIAL REPORT FOR THE ICH COMMITTEE

July 1, 1949, to Sept. 30, 1949

Balance on hand June 30, 1949			$33,268.43
Receipts			
Charles H. Hood Foundation			1,000.00
Albert H. & Jessie D. Wiggin Foundation			2,500.00
			$36,768.43
Disbursements			
Salaries	$ 8,545.34		
Rent	853.14		
Travel	421.04		
Postage	363.93		
Insurance	23.27		
Express	2.61		
Office Expense	92.03		
Telephone and Telegraph	224.84		
Meetings	365.00		
Miscellaneous	9.80		
Periodicals and Books	42.55		
Car Maintenance	181.52		
Petty Cash	503.83		
Additional Copies of Study Report by Auditors	25.00		
Publicity and Public Relations Counsel	1,666.68		
Publicity Expense	65.02	13,385.60	
Credit on Petty Cash checks spent prior to June 30, 1949		503.78	12,881.82
Balance on hand Sept. 30, 1949			$23,886.61

The following is the simplified Treasurer's Report as suggested by Dr. Martmer:

AMERICAN ACADEMY OF PEDIATRICS
STATEMENT OF EXPENSES

July 1, 1948, through June 30, 1949

Total Budget	$64,050.00
Total Expenses	58,179.98
Savings over Budget	$ 5,870.02

STATEMENT OF BUDGET ALLOWANCE AND ACTUAL EXPENDITURES

	Budget Allowance	Actual Expenditure	Savings
Evanston Office	$45,550.00	$44,874.15	$ 675.85
Executive Board	8,000.00	10,194.57	**Deficit 2,044.57
Secretarial Allowances (Executive Board and State Chairmen)	1,000.00	491.54	508.46
Special Committees	3,000.00	2,619.72	380.28
Contingency Funds	6,500.00		
Total	$64,050.00	$58,179.98	

BUDGET ALLOWANCE AND ACTUAL EXPENDITURE

Evanston Office

July 1, 1948, to June 30, 1949

	Budget Allowance	Actual Expenditure	Savings	Excess Expenditure
Salaries				
Officers	$23,000.00	$23,000.00	$ —	$ —
Staff	11,000.00	10,635.84	364.16	—
Rent	3,000.00	2,757.68	262.38	—
Travel	1,500.00	1,631.34	—	131.34
Printing and Postage	4,700.00	4,167.43	532.57	—
Operating Expenses	2,350.00	2,701.92	—	351.92
Total	$45,550.00	$44,874.15	$1,159.11	$ 483.26

ITEMIZED STATEMENT OF EXPENDITURES

Evanston Office

	Budget	Actual Expenditure
Salaries		
Secretary	$18,000.00	$18,000.00
Ass't Secretary	5,000.00	5,000.00
Staff		
Office Manager	5,000.00	5,000.00
Secretaries	6,000.00	5,635.84
Rent	3,000.00	2,737.62
Travel—Secretary	1,500.00	1,631.34
Printing and Postage		
Stationery and Printing	3,500.00	3,263.29
Postage	1,200.00	904.14
Operating Expenses		
Treasurer's Bonds	350.00	322.50
*Office Supplies & Equipment	500.00	893.34*
†Incidentals	1,500.00	1,486.08

* Excess Expenditures due to Purchase of Additional Equipment Authorized by Executive Board.

	Budget	Actual Expenditure
† Incidentals	$ 1,500.00	$ 1,486.08
Bank Charges	$ 73.36	
Certificates of Membership	168.18	
Telephone and Telegraph	583.01	
Miscellaneous	661.53	
	$1,486.08	

The following District Reports were presented and accepted:

District 1: The Fellows of the Academy in Connecticut, Rhode Island, Massachusetts, New Hampshire and Vermont have organized themselves, and they have elected their own State Chairmen. Connecticut and Massachusetts have an Executive Board consisting of 6 men who meet with the State Chairman on all matters pertaining to Academy business and child problems of the state. This arrangement has enabled the State Chairmen to keep the members of the Academy well informed on all Academy activities.

The Preliminary Report of the Committee on Reorganization was sent to each State Chairman, who, in turn, studied it in detail with his Executive Committee or the other members of the state

and gave their constructive ideas and criticisms. These were immediately forwarded to the Reorganization Committee.

The following are reports of the State Chairmen themselves:

Dr. J. Harold Root of Connecticut reports as follows:

1. The Child Care Study and report for Connecticut has been published and distributed. 2. $1,000, borrowed for the National Child Care Study in Connecticut, has been repaid to the Academy. 3. A state-wide committee is being organized to carry out recommendations of the study and promote increased interest in child health. 4. Several Child Care conferences have been held and others are being promoted by P.T.A. groups, Women's Auxiliary of the State Medical Society and other organizations.

Dr. J. Harold Root has been State Chairman since 1943 and last year was elected for a 3 year term. Since the completion of the study, he has resigned and the Fellows have elected the Alternate Chairman, Dr. John B. Griggs of Hartford, to fill his unexpired term. Dr. Root has done an exceptionally fine job as State Chairman. He has offered the benefit of his experience to Dr. Griggs and to his Executive Board. We can justly expect capable leadership from Dr. Griggs.

Dr. James M. Baty of Massachusetts reports as follows:

"Our report of the Study has been published. A summary of this report has just appeared in the Sept. 22 issue of the *New England Journal of Medicine.*

"We are planning to have the annual meeting of the members of the Massachusetts Chapter of the Academy on Oct. 19. At that time we hope to have appointed a child health committee to develop, in collaboration with medical, dental and other health organizations, a program for the improvement in and better distribution of health services for children in Massachusetts.

"The Committee on Fetus and Newborn has been active particularly in helping to obtain better laws for the care of premature infants in the state."

Dr. Robert M. Lord of Rhode Island reports as follows:

"There are so few members in the state of Rhode Island that we all acted as a committee in editing the *Child Survey for Rhode Island* for local consumption. We divided up the report among committees of 3 members who consulted with the local state and city health departments, the district nursing association, officials of the hospitals and members of charitable organizations. We have now completed this survey and the *Rhode Island Medical Journal* has agreed to publish it in one issue. We are having reprints made which will be sent to public libraries, colleges, health departments and health offices, charitable organizations, hospitals and possibly senior high schools. There will also be copies for distribution outside the state for those who are interested.

"Most of the credit for the completion of this survey should be given to our former State Chairman, Dr. William P. Buffum, but the rest of the members and the organizations mentioned have all contributed their time and effort."

Dr. Paul D. Clark of Vermont is working with the Medical School of the University of Vermont, the State Medical Society and the Board of Health in Child Care matters. Dr. Clark has been elected by the Fellows of Vermont as their State Chairman for 3 years.

Dr. Colin C. Stewart of New Hampshire reports as follows:

"Our activity, as usual, has been as individuals rather than as a group. During the Spring, Dr. Barbara Beattie, Dr. Thomas Walker and Dr. Douglass Walker served with me on a committee to advise the State Department of Education about health matters, particularly relating to the school examinations. I have just been asked by the Governor to form a committee to see what can be done about the 1950 White House Conference on Child Welfare. I hope some of my pediatrician friends will be able to help me out on that assignment."

Dr. Albert W. Fellows of Maine reports as follows:

"The only Academy activity so far this year has been the report which is now nearly completed. The Committee on Fetus and Newborn is formed and includes an obstetrician. It is developing a plan of action.

"Other activities are planned."

Respectfully submitted,

OLIVER L. STRINGFIELD, M.D., *Chairman*

Motion was made, seconded and carried, that the $1000 refund by the Connecticut Chapter be accepted by the Academy.

District II: Since the last meeting of the Executive Board, there have been no official meetings of the membership in our district. However, there have been many informal gatherings discussing the future work and aims of the Academy.

On Sept. 28 in New York City, there will be a meeting of the Fellows from the metropolitan districts which has been called by Dr. Givan and Dr. Wilke and will be held in the Academy of Medicine. At this meeting, I will review the activities of the Executive Board within the last 2 years, after which there will be a general discussion and opinions expressed not only by the chairmen but by those of the membership who are in attendance.

Similarly, on Oct. 27 there will be held in Rochester a meeting of the Academy membership for upper New York State. At that time, I will repeat the report to be given in New York and there will be a general discussion, which will be led by the upper New York State Chairman, Dr. William Orr.

Respectfully submitted,

PAUL W. BEAVEN, M.D., *Chairman*

District III: New Jersey reports that the State Chapter has been organized and officers nominated as follows: Dr. Frederic W. Lathrop, Plainfield, State Chairman, Dr. William F. Matthews, Montclair, Alternate State Chairman and Dr. Walter Mitchell, Newark, Secretary Treasurer, all to be in office for a term of 3 years. The New Jersey state report of the Survey is finished and published.

The Rheumatic Fever Committee has been active and established a demonstration convalescent cardiac clinic.

The Mental Health Committee has published a comprehensive reference list of books on child psychology.

All the work of the Academy is carried on in close cooperation with the Medical Society of New Jersey.

Delaware, while a small chapter, is active in promoting pediatric programs throughout the state. The State Survey report is still in composition.

Pennsylvania's Western Chapter has organized and elected W. W. Briant, Jr., as State Chairman for the next 3 years. The Eastern Chapter is to hold its organization meeting in October, too late to be included in this report. The Pennsylvania Survey report is still in composition.

Dr. Elizabeth Rose has been active in the work on neonatal mortality in Philadelphia and trying to stimulate adequate reports and studies on infant deaths.

The District III program of decentralization is progressing. Many hospitals are interested but lack of adequate finances prevents full scale operation. However, by the November meeting, the first actual operations will have started. The search for funds continues.

The stimulation and enthusiasm produced by the Child Health Survey has not yet died out. Many of the Fellows are anxious to push on to better things.

Respectfully submitted,

PHILIP S. BARBA, M.D., *Chairman*

District IV: The areal meeting held in Atlanta, Ga., in April was highly successful. All those attending considered the scientic program to be excellent. It might be of interest to the membership of the Academy to know that the scientific program for this and other areal meetings is gotten up entirely by the local program committee. In the case of this areal meeting, the local committee was ably headed by Dr. Joseph Yampolsky. The membership of the State of Georgia, through their State Chairman, have written me that they consider it an honor to have entertained the Academy and will welcome the opportunity to have a meeting in Atlanta again in the near future.

A summary of the activities of the various State Chapters in this District follows:

Maryland (Dr. Paul Harper, State Chairman): In this state the members of the Academy have organized a Chapter and adopted a Constitution and By-Laws. There have been 8 applications for membership from Maryland since the last annual meeting. Eighteen pediatricians in Maryland have been certified by the American Board of Pediatrics in the past year and the State Chairman is making efforts to have these become members of the Academy. The Maryland Study of Child Health Services has been completed and the report is in the process of being written at the present time. The Premature Mortality Committee, under the leadership of Dr. D. C. Wharton Smith, is continuing its

activity in the State and the members of this group constitute the Committee on Fetus and Newborn of the Academy in Maryland.

District of Columbia (Dr. Edgar P. Copeland, State Chairman): The report of the Survey of Child Health Services has been completed and is now in press. The Pediatric Department at Howard University has succeeded in securing departmental status for pediatrics under the direction of Dr. Scott. Dr. Scott was aided in this accomplishment by Academy members in the District of Columbia. The City Hospital (Gallinger) has begun construction of a new pediatric unit of 100 beds which is under the direction of Dr. Sweet. The Children's Hospital in Washington is planning new construction to add to their present facilities.

Virginia (Dr. Emily Gardner, State Chairman): There have been 3 applications for membership in the Academy since the last annual meeting. The Committee on Fetus and Newborn of the Academy, in conjunction with the Virginia State Department of Health and the Department of Continuation Education of the Medical College of Virginia, presented an institute on prematurity in October 1949.

North Carolina (Dr. Charles R. Bugg, State Chairman): There have been 2 applications for membership from this state. The chief activity of the membership this year has been directed towards completion of the Premature Care Program. Completed units now number 4 with 2 more units in the State nearing completion. Three hundred thirty-four cases were authorized between July 1948 and July 1949. Of these, 172 have been discharged and considered closed. The over-all mortality has been 8.7%; average number of days in the hospital, 30; average cost per patient, $444.21 in 1948 and in 1949, $430.16. The State Chairman had a conference with the Secretary of the State Board of Medical Examiners and feels that the pediatric portion of the State Board Examinations is as satisfactory as can be arranged. A business meeting of the pediatricians was held in May 1949 and a scientific session was held in September 1949, at which time the group was addressed by Dr. Waldo Nelson of Temple Medical School.

South Carolina (Dr. William Weston, Jr., State Chairman): There has been 1 new member of the Academy admitted from South Carolina during the past year. The South Carolina Pediatric Society met in September 1949 and was addressed by Dr. John Toomey and Dr. Irvine McQuarrie. The meeting was reported to be highly successful. The South Carolina Report of Child Health Services has been completed.

Georgia (Dr. William W. Anderson, State Chairman): Two new members have been admitted to the Academy from Georgia. The Child Health Services Report was completed in April and has been distributed. An ideal premature nursery has been established at the Crawford Long Hospital in Atlanta. The State Chairman reports that only a small per cent of the pediatricians in Georgia are members of the Academy, but that the Academy members serve willingly on any committee and he feels that the Academy in the state is well-organized.

Florida (Dr. James B. Boulware, State Chairman): Two new members have been admitted from Florida. The State Chairman reports that no follow-up on the Academy Study has been attempted, but that plans are being made to begin work at the October meeting of the Pediatric Group. The membership of Florida is saddened by the death of Dr. George Cook, past State Chairman, who had served the Academy well for many years.

West Virginia (Dr. Russell C. Bond, State Chairman): There has been 1 new member from West Virginia. During the past year, the chief activity of the members was preparing the Study Report for publication. A final draft has been written and is now in the process of printing.

During the past year several pediatricians in the state have passed the Board examination and will soon be eligible for election to the Academy.

At the last meeting of the West Virginia State Medical Association, the House of Delegates accepted the report of the Study and voted that the Child Health Committee of the West Virginia State Medical Association carry on the recommendations given in the Study Report. They also expressed their willingness to cooperate with the Academy in carrying out its projects dealing with Child Health.

Puerto Rico (Dr. J. Roberto Aguayo, State Chairman): No report has been received from the State Chairman of Puerto Rico.

With the exception of Maryland and the District of Columbia, there are no large groups of Academy members in any one locality in District IV so that it is rather difficult to show uniform

action on the part of Academy members in any one location. However, your District Chairman feels that the Academy members are interested in the work and are willing and cooperative and that the state of the Academy in District IV is good.

Respectfully submitted,

ARTHUR H. LONDON, JR., M.D., *Chairman*

District V: Continuing from the last report of District V supplied by Dr. Hoyer at the June meeting of the Executive Board in Chicago, it is my privilege to report on the progress which has been made to date.

The work on the decentralization of the Academy activities has resulted in the States of Ohio and Michigan having formed State Chapters of the American Academy of Pediatrics and adopting constitutions. These State chapters will meet at least once a year and it is planned to meet in conjunction with the State Medical Society meetings. This will enable closer cooperation with the State societies and, through them, with the A.M.A. on a state level, which is to be desired.

Provision has been made in Michigan to invite nonmembers to participate in the Chapter meetings. This has been done in the hope that it will act as an incentive for the nonmembers of the Academy to become members.

The same has been planned for Indiana and a meeting of the Indiana pediatrists has been called for Oct. 15 at South Bend to organize and adopt a constitution. This leaves only Ontario and Kentucky as yet unorganized into local state or provincial chapters and, I assure you, every effort will be made to organize these areas along the same lines.

The most important activity of the District, however, resulted from a meeting of the State Chairmen held in Ypsilanti, Mich., Aug. 14, 1949, which was attended by all State Chairmen of the District except Ontario. At this meeting, there was long and deliberate discussion of the reorganization committee's report, which had been forwarded to the District Chairmen. The following letter, signed by each State Chairman present, was sent to the President of the Academy and also to every other State Chairman in the other districts and is herewith presented for your consideration:

"The State Chairmen of District V meeting at Ypsilanti, Mich., Sunday, Aug. 14, 1949, in response to a call by Dr. Edward Wishropp, the District Chairman, reviewed the report of the Committee on Reorganization of the American Academy of Pediatrics.

"After a full and detailed consideration of the committee report and the many problems involved, we reached a unanimous decision as to the following conclusions:

"1. In view of the critical attitude and unrest among the membership of the American Academy of Pediatrics at the present time, together with the limited funds available, we feel that plans for reorganization should be thoroughly publicized to the entire membership with ample time for their consideration before adoption.

"2. We believe that the present Committee for the Improvement of Child Health should be discontinued. To correlate all the child health activities of the Academy, we propose the establishment of a committee composed of the Chairmen of the Standing Committees to be known as the Child Health Committee. The purpose of this committee would be to serve as a correlating and advisory committee solely and not an action planning committee.

"3. We believe that the present division of committees into Standing and Special Committees is a logical procedure and should be continued. When a committee has fulfilled its function, it should be disbanded. If a new problem arises, a suitable committee should be established.

"4. We are moved to ask what justification there can be for disbanding all present committees and the appointment of new committees to perform the same function.

"5. We see no justification in the additional expense which would result from the employment of a part-time physician to assist the Program Committee. This function we feel has been handled efficiently up to the present time by the Academy Office.

"6. The Central Office Staff should include a Business Manager to assume such duties as are assigned by the Secretary-Treasurer.

"7. The consensus of opinion of the State Chairmen of District V is that Public Relations is an extremely important field. We feel that not only is it important that the views of the membership of the Academy be made known to others but that full information on all matters should be presented to the membership promptly.

"In this connection it is our feeling that a Public Relations organization of national scope working in close cooperation with the Secretary-Treasurer would provide many advantages over a single individual employed by the Academy.

"8. It is our studied opinion that the office of Secretary-Treasurer should not be abolished. He should direct all activities and business of the Academy subject to the approval of the Executive Board.

"9. To provide for emergencies and eventualities we believe an understudy to the Secretary-Treasurer should be trained who would be capable of assuming the duties of the Secretary-Treasurer on short notice. Continuity of service is essential for the efficient management of the activities and business matters of the Academy.

"10. We question the advisability of the Executive Board's adopting any report of the Committee on Reorganization before such an important matter has been presented to the Academy members to permit ample opportunity for full discussion and expression of opinion to their State and District Chairmen.

Fraternally yours,
(signed) Frank Van Schoick, M.D. (Michigan)
Ernest R. Carlo, M.D. (Indiana)
James G. Kramer, M.D. (Ohio)
William W. Nicholson, M.D. (Kentucky)"

The replies from this letter have been many, and in most cases have shown that the other districts are generally in agreement with the recommendations contained in the letter.

I am glad to report also that there have been submitted the names and completed application forms of 23 candidates for Fellowship in the Academy from District V.

Respectfully submitted,

EDWARD A. WISHROPP, M.D., *Chairman*

District VI: Reports have been received from all states and provinces of the District.

Dr. John C. S. Brown of Saskatchewan reports that the number of pediatricians in the province has increased to at least 10 and that they are receiving recognition in the health activities of their province. At the present time, only 6 of these men are listed as specialists. Dr. Brown is the sole member of the Academy in his province. So far, the pediatricians have not been well organized and have not worked together. Dr. Brown looks forward to the day when they will have much more voice in the work of child welfare in that area. In a meeting of the Canadian Medical Association at Saskatoon, this organization went on record as opposed to socialized medicine and approved the establishment of voluntary prepaid medical care, both for hospital and physician's services.

Dr. Harry Medovy of Manitoba reports that Academy members in his province are active in postgraduate work and in assisting the provincial government in examination of spastic children as part of a survey. Dr. Medovy himself has been instrumental in the examination of well water in various areas for nitrate content. There are 3 members of the Academy in the province of Manitoba.

Dr. Roland E. Nutting of Minnesota reports that their state Academy organization has now been perfected and that the first meeting was held on Aug. 6, 1949. As a result of this organization, it is felt that the Academy activities of the state can be administered much more efficiently. A committee has been formed to implement the findings of the Child Health Study. This committee is composed of Dr. George Logan, Chairman of the State Child Health Committee; Dr. Rosenfield, Maternal and Child Health director; Dr. Elias, President of the state association; Dr. Victor O. Wilson, Executive Secretary in the preparation of the state report; Dr. W. A. George, Dental Health director of the Minnesota Department of Health; and Dr. Nutting.

Dr. James E. Dyson of Iowa reports that the Iowa State Pediatric Society met in Iowa City on Oct. 11 and 12 as guests of the Iowa State University Medical School. The Child Health Survey was published in the September issue of the *Journal of the Iowa State Medical Society* and reprints are being prepared for distribution.

Dr. M. G. Peterman of Wisconsin included in his report much of the information that he had reported previously for the June District Chairman's report. In addition, he reported that Dr. Winthrop Phelps had held clinics and lectures on cerebral palsy in children at the state meeting of the

Wisconsin Medical Society on Oct. 4, 5 and 6. The pediatric group is now making efforts to obtain representation on the state board of medical examiners. The committee appointments that were made during the past year have been Dr. H. Kent Tenney, Jr., Chairman of the Child Health Study Committee, Dr. F. J. Mellencamp and Dr. J. R. Schroder. The Committee on Safety and Accident Prevention is composed of Dr. James P. Conway, Chairman, Dr. George H. Wegmann, Dr. H. A. Sincock and Dr. L. M. Simonson.

Dr. Eugene T. McEnery of Illinois reports that the State Child Health Survey Committee will hold a meeting early this fall in order to expedite early publication of the Child Health Study reports in the State Medical Journal. Dr. Gerard Krost, Chairman of the Committee on Fetus and Newborn, reports that they have been working on a plan to submit to the Chicago Pediatric Society at its first meeting in October, whereby a pediatrician is to be in charge of every newborn nursery in Chicago. This plan will also be submitted to the Chicago Medical Society and, if approved, will be taken before the Chicago Health Department for its approval.

Dr. Goldie E. Zimmerman of South Dakota reports that she has contacted all members of the state board of examiners and the superintendent of the State Health Department in regard to having a separate pediatric examination and has requested that the questions be framed by a pediatrician.

Dr. J. Harry Murphy of Nebraska reports that at a recent meeting of the Academy members, special discussions were held concerning milk laboratories and also on the care of premature infants and on rheumatic fever problems. At this same meeting, an invitation was extended to the Academy through Dr. Grulee to hold the National Meeting in Omaha in 1951. The Academy survey of medical health services in Nebraska will soon be in the hands of the printers.

Dr. Ralph Dyson of North Dakota reports that the state pediatric society has been organized and includes the 9 pediatricians in the state and 25 associate members. This group plans to have 2 meetings each year.

Four applicants for membership in the Academy have presented proper credentials and will be voted on at this meeting.

Respectfully submitted,

GEORGE F. MUNNS, M.D., *Chairman*

District VII: All the states have or are in the process of completing their Chapters.

The Child Health Study is bearing fruit. There are several states in our District to complete their State Reports. Louisiana deserves the greatest credit within our District for the immediate application of the results of the Child Health Study. The illustrated manual of "What We're Doing for Our Children" is a complete, simplified story of the Study; put together with pictures and statistics that are easily understood by the general public, it will go a long way toward bringing the needs of children to the attention of the Legislators.

Louisiana has a State School for handicapped children in Alexandria, giving service particularly to spastics. This school has been functioning a little over a year and apparently is working successfully. The Hearing Clinic of the Eye, Ear, Nose and Throat Hospital in New Orleans has recently completed its first year of operation. The Shreveport Child Guidance Center has been functioning effectively for 2 years and a third Child Guidance Center has recently been established in Baton Rouge. A school for handicapped children and a special class for deaf and partially deaf children have been established in the Shreveport Public School system with considerable financial assistance by a local Society for Exceptional Children. The regular Crippled Children's program, under the auspices of the State Department of Health, had been handicapped during the early part of the year because of a shortage of funds but now seems to be functioning adequately.

The Missouri State Pediatric Society appointed a liaison committee to work with the State Committee on the Care of Infants and Newborns. The Committee appointed was Dr. George V. Herrman, Chairman, Dr. Daniel B. Landau and Dr. Harold E. Petersen. Through its new constitution, it has markedly improved the adoption regulations in the large cities where members of the Academy have, in the last year, actively participated in development of excellent adoption programs for legitimate agencies. The State Chairman reports, however, that it is regrettable that from the law's standpoint, the child is not sufficiently protected, so far as health is concerned, during the 9 month probation period in which he may be in a home for formal adoption. This serious deficiency, which is apparently more or less national, could well be a subject for the Academy on a national level.

Mississippi has had a satisfactory juvenile delinquency law for a good many years. They also have many Children and Youth Committees, most of them working under the supervision of the Public Health Department.

Plans are being made in Tennessee for the organization of a postgraduate course in pediatrics, to be given over the state by an instructor who, on a regular program, will give seminars. Money for this has not yet been obtained. More strict laws regarding the adoption of babies have been passed.

At Vanderbilt University, a center for crippled children with physiotherapy, speech and occupational therapy and a 20 bed polio unit have been established. New premature nurseries have been built and 2 postgraduate courses a year have been organized, the first of which will be given in October.

At the University of Tennessee, the following have been initiated: an Epilepsy Clinic, a Speech and Hearing Center, a 16 bed Cerebral Palsy Unit, and a Heart Clinic. Four new nurseries have been built in a new addition to the Maternity building at the John Gaston Hospital to replace the old smaller ones. Some of the residents at John Gaston Hospital rotate on the services at the St. Joseph's Hospital and the Baptist Hospital. A consultation service from the Department of Pediatrics for the counties in North Mississippi is in operation and plans are under way for the establishment of an outpatient department for crippled children in a newly acquired building which will open in December.

The Tennessee Pediatric Society, which is practically the Tennessee chapter of the Academy, and the State Board of Health are organizing committees in each county for the improvement of child health, with the first effort directed to the improvement in newborn and premature care.

Texas University now has a School of Social Service which has long been needed and will greatly benefit the Texas children in the future. The Committee of Children and Youth has been active in co-ordinating the activities of approximately 40 organizations within the state. The Texas State Youth Development Council was established by the last Legislature. It has 3 training schools under its jurisdiction and a program of child care with a full-time director has been set up on a local level from all points of view—courts, schools, playgrounds and a diagnostic center cooperating. A Public Relations Director, who is also full-time, has the responsibility of the prevention of juvenile delinquency. The Mental Health Division within the State Health Department is now 2 years old. It has a full time Director, Dr. Elizabeth F. Gentry, who is an Academy member. This Mental Health Division has 2 worth while programs in operation. One is the Well Child Care, the other the School Health program. There are 3 Mental Health clinics, all of which take at least 60% children, located in Dallas, Ft. Worth and Houston. Plans are already made for the establishment of one in Austin.

A postgraduate course in Child Development and Mental Health will be held at Baylor Medical School for 1 week for pediatricians.

We feel that Texas has made great strides in the care of premature infants. This last year, 3 Premature Nurseries have been established and are being used as training centers. They are located in Austin, Dallas and Galveston.

Practically all the states in District VII have continued to have refresher courses in pediatrics.

It is with a great deal of sorrow that we report the death of Dr. Paul E. Belknap, State Chairman of Kansas, who died of a coronary on Aug. 29, 1949.

Respectfully submitted,

THOMAS J. MCELHENNEY, M.D., *Chairman*

Motion was made, seconded and carried that the Executive Board recommend to the Business Session of the Academy meeting that at the expiration of the terms of the present State Chairmen, in those states that have 2 or more State Chairmen, there hereafter be only one State Chairman, with the privilege of having as many Vice Chairmen as the state chapter deems necessary to carry on the business of the Academy in that state; and further that in each state there be an Alternate State Chairman with full power to take over in the event of any incapacity or other circumstance which prevents the State Chairman from serving.

District VIII: Activities listed by the state chairmen are many. It would appear that the chairmen, as well as many of the members, are taking part in activities in all the fields that concern child health. The state chairmen were recently acquainted with the primary proposals of the Reorganization Committee and have made constructive suggestions to this committee.

Some states are in the process of organizing state chapters in order to provide a better medium for

the discussion of the Academy affairs. Elections this year brought 6 new chairmen into office. All these men have been heard from and are actively enthusiastic.

Respectfully submitted,

CRAWFORD BOST, M.D., *Chairman*

Upon motion made and seconded, the following District Elections were accepted by the Board: District I: Alternate District Chairman—Dr. Lendon Snedeker, Boston, Mass.; District III: District Chairman—Dr. Philip S. Barba, Philadelphia, Pa.; District IV: Alternate District Chairman—Dr. Preston A. McLendon, Washington, D.C.; District VI: District Chairman—Dr. Roger L. J. Kennedy, Rochester, Minn., Alternate District Chairman—Dr. Eugene T. McEnery, Chicago, Ill.; District VII: Alternate District Chairman—Dr. James Carney Overall, Nashville, Tenn.

The following reports of Standing Committees with State Activities were presented:

REPORT OF THE COMMITTEE ON COOPERATION WITH THE AMERICAN LEGION

More than 20 years ago the American Legion invited the Academy of Pediatrics to establish a liaison relationship with the National Child Welfare Division of the Legion. This was done in order to make available to the Legion the advice of qualified child specialists on problems of child welfare having a bearing on the health of American children. The Academy of Pediatrics established a Committee for Cooperation with the American Legion to perform this function.

Through the years a happy relationship has existed between the 2 organizations. The Academy's committee has cooperated well with the Legion in an advisory capacity and it is felt by both groups that the liaison arrangement has been fruitful, but on a limited plane only.

The physical incapacity of Dr. Edward Clay Mitchell, who had originated the idea of the cooperative effort between the 2 groups, and the disruption of World War II greatly lessened the effectiveness of the arrangement. Dr. Mitchell had put a great deal of effort into making the plan work, and his loss through illness deprived the Academy of a most effective representative.

Dr. Hugh McCulloch took up where Dr. Mitchell had left off; he succeeded in getting groups of the American Legion at the national level to allocate $50,000.00 for the study of heart disease. This was one of the most productive accomplishments of the liaison between the Academy and the Legion.

At the conclusion of the war, the decision was made to reorganize the Committee on Cooperation with the American Legion so that younger members of the Academy who had served in the armed forces would take the responsibility for the program. This was done, and the present Chairman of the committee took office.

District Liaison Officers were appointed for the 8 U.S. districts of the Academy and they in turn appointed State Liaison Officers in almost all the states of the nation. The purpose of these district and state officers was to stand ready to advise on any of the Legion's state or area child welfare plans which might have a bearing on the health of children. Each state in the country has its American Legion organization and an American Legion Child Welfare Committee. The Women's Auxiliary of the Legion, the fraternity of the Legion, called the "Forty and Eight," and the sorority of the Legion, called the "Eight and Forty," also have their child welfare committees. The 4 groups of the Legion plan their child welfare work jointly by blending themselves into what is called a "Coordinated Committee." It was considered likely that these coordinated committees throughout the country would seek advice and help in their planning by consulting with the Academy's state or district liaison officers.

Although theoretically correct, nevertheless, the plan did not work. The state child welfare chairman of the Legion rarely sought advice and in some instances did not seem to know of the existence of the Academy's representatives. Lists of the Academy appointees had been sent forward to Legion Headquarters. However, the policy of the Legion does not permit the National Child Welfare Division to tell the state Child Welfare Chairmen what to do. Very little has come so far of this liaison at the state level.

Meanwhile, the Academy of Pediatrics was conducting its Study of Child Health Services and Pediatric Education, which revealed so clearly the startling deficiencies in child care in our nation. Everyone knew the patient was sick, but the survey clarified the diagnosis. For the first time the facts were obtained upon which to base any future action.

The Academy appointed its Committee for the Improvement of Child Health for the purpose of planning methods to increase the quality and better distribution of child care and to recommend ways to strengthen pediatric education. In spite of differences of opinion among Academy members as to what should be done and how to go about it, the general belief prevails that the Academy has a moral responsibility to the children of the nation to try its level best to bring about a correction of the widespread intolerable situation that prevails in regard to child health and pediatric education. If ever statistics had vitality, those facts brought out by the Academy's survey live and breathe and tell a story full of deep meaning. It is impossible for a sensible person and one sensitive to human needs to see what is wrong and not to take action. It would be callous beyond belief for an Academy like ours, with all of its national prestige and responsibility for leadership, to sit upon this mass of facts and idly contemplate the scene. Something must be done because something needs so badly to be done.

A great barrier to effective action has been the widespread fear and distrust of the increasingly socialistic trends in government, especially as they have a bearing on medical services. Socialized medicine is not consistent with the best quality of medical care, and the vast majority of the Academy's membership is unalterably opposed to it, as is the writer. The answer to getting the job done lies not in Washington, but in the intelligent and energetic action of state pediatric groups who have the moral responsibility to try to correct what is wrong in their own areas, and who know best how to solve their own problems. The function of the Academy at the national level should be to inspire the state pediatric groups and other organizations to start programs to improve child care in their areas, and to give advice and counsel when requested to do so. No matter what methods are adopted by the various state groups to improve child care, there will be a continuing need for the Academy to maintain at a national level the personnel and facilities who will be invaluable in helping plan programs, in assisting the pediatric groups to go about their work more effectively, in giving the states the proper publicity on a national scale, and in critically analyzing the accomplishments through the year.

The Academy cannot be expected to solve the child care situation by itself. That would require more pediatricians and more money than we are likely ever to see in our own group. The Academy should take the initiative in enlisting the services of all organizations and groups interested in children to the end that the job will be done by cooperative planning and joint effort.

If we take the leadership, as we should, it will be of great importance to know who our friends and fellow-workers will be. We need to team up for action with organizations that are not only strong at a national level but which have powerful state groups capable of implementing the planning. We need to work with organizations which have already been active in the field of child health and whose past records give promise of future accomplishments. In the framework of private enterprise the job can be done. Forces for better child health are already in action and on many fronts. We can help coordinate those forces by wise planning and friendly cooperation. Latent forces now dormant can be aroused, and people and money can be obtained to help us build for better health.

The longer we wait, the worse our situation becomes and the greater the threat that a plan and a program will be rammed down our throats by legislative action. We do not want this, but a vacillating approach to the problems at hand will only hasten the day when someone else will be doing the job the Academy is so eminently fitted to do. The job will be less well done and the Academy will have lost a golden opportunity to serve the children of the country. What lies ahead can either be our finest hour or our worst defeat.

We have passed through the phase when high talk of altruistic aims sufficed to indicate our good intentions. The situation does not now permit, nor will the public long condone, any further delay in tackling the problems at the state and local level, as well as on the national plane.

In this critical state of affairs, when so much is at stake for the children of the nation and for the Academy itself, the American Legion has come forward with a Community Development Program of which one important phase is child health (see attached resolution). Much of the wording of the proposed Child Health Program reflects the influence the Academy has already exerted through a conference with representatives of the Legion Child Welfare Division at the offices of the ICH Committee last June. It is anticipated that Legion posts throughout the country will make earnest efforts to pool community resources to the end that many phases of community life will be enriched. There is a fine opportunity here for the Academy to join in and assume some of the leadership in planning for better child health. The American Legion has asked the Academy to do this and it is recommended that we give all the help we can. The AMA has also been asked to cooperate in the program through

its Physical Fitness School Health programs, as well as in the very important Health Education program involving all sorts of powerful publicity. The American Dental Association, the American Hospital Association, and other groups as well are being asked to join. As an Academy, we are being asked to change our relationship to the Legion from a purely advisory one to one of joint action on common problems.

There is much that we can do to make the plan work. If state pediatric societies made the efforts necessary to meet with and plan with state Legion authorities and representatives of other groups, and if this were repeated in the communities of the states, much might be accomplished. Large sums of money now being spent by the Legion on many projects of less importance than child health might be diverted to better use. Additional funds might be raised. Where indicated, the powerful legislative forces of the Legion might bring about needed changes in state laws insofar as they have a bearing on the health of children. One need not expand on the possibilities, for all of us know what concerted action on any problem can achieve.

It would be a great mistake to assume that the American Legion, or any other organization, has such strength in all sections of the country that it would be invariably the natural leader in bringing about community planning for better health. While there are several million members and many thousands of Legion posts, the Legion is strong in some areas and not so strong in others. The Academy has a similar situation with regard to state pediatric societies. It is quite probable that in some areas of the country real leadership might come from other groups. It really does not matter from whence it comes so long as it comes in the right form.

It would also be a mistake to assume that this program would not be full of growing pains. The organizations listed have had little experience working with one another on such a large scale. Some sections of the country would get results much faster than others. Where physicians are few and distances are great, there would be great obstacles to progress. In some of the larger urban areas, community planning for better health has already reached a high peak and it is not anticipated that great changes would be indicated.

Equipped with the armamentarium of its survey, the Academy is in a fine position to spark this program. From the very facts brought out by the survey, the Academy, at a national level, might select a few key areas where such a program would be most needed and most likely to succeed. The Academy could then stimulate the state pediatric societies of those areas to assume leadership in the program. The Academy could be of invaluable assistance in an advisory capacity to the state pediatric societies, as it was during the stages of the survey. At a national level, the Academy could stimulate cooperation from the other agencies listed, to the end that these national organizations could in turn stimulate their state groups to take an active part. Given the wholehearted cooperation of all the agencies at the state level, there is no shadow of a doubt but that great gains would be achieved. When these pilot programs in carefully selected areas had been shown to succeed, it would be increasingly easy for other areas, using the knowledge gained, to take up their programs.

The plan sounds big and it is big. It offers vast prospects and it entails vast efforts. However, when it is broken down into its component parts at the state and local levels it will not seem so large. It does not call upon us to do anything which we are not already well equipped by training and experience to do. Of all the organizations working together, we should be best prepared for our part. This is true because our minds have been focused on this problem so intently through the survey and the demonstrated needs.

If the Academy accepts the invitation made by the Legion, as it should, it is recommended that the state pediatric societies be the agencies to work at the state level with the Legion.

It is further recommended that the entire group of liaison officers be disbanded. There will be no need for their services and to retain them would lead to duplication. The Academy's present framework of state chairmen and state societies is sufficient for the task ahead.

The future of the ICH Committee would be greatly influenced by the program contemplated. If we manage this opportunity wisely, the needs for such a committee will be multiplied many fold. There will have to be a group of Academy members at the national level whose function it would be to keep the liaison with other national organizations alive, and this will require personnel and money. The ICH Committee, or at least personnel whose sole function it is to stimulate an improvement in child health, will be indispensable. While some few very active state pediatric societies might initiate action and accomplish a great deal, too much hangs in the balance to place the sole responsibility at a state level. Also, we must not forget that such a central committee might be most instrumental in obtaining funds at a national level to help in areas of need.

Such a committee would be of real value in analyzing the information which will be arising from such joint efforts. Programs will need to be analyzed, plans for action will need to be written up for use by state societies on request, and the over-all accomplishments will need to be catalogued.

The opportunities for publicity favorable to the program itself and redounding to the credit of the Academy should not be missed. Here is a chance to make the most of work well done. Given the right efforts and the right publicity, the American people will see that private enterprise can be effective, that physicians are aware of the socio-economic aspects of medical care, and that a concerted effort is really being made to establish a better brand of child health. The ICH Committee, or a similar group, would have many a fine opportunity to help the program and to help the Academy.

If the Academy does not see fit to join in this cooperative effort with the American Legion and other organizations, I see no reason to continue the liaison relationship with the Legion. If we are not willing to work with them on a program which has such prospects of accomplishing so many common objectives, then we do not have enough in common to justify a continuation of our relationship. I do not believe that the Academy will miss this opportunity. I believe that clear thinking will penetrate the maze of difficulties ahead, and lead us to the decision that this proposed program is a long step in the right direction.

I recommend that the Academy endorse the idea in principle and that it set about immediately to make the necessary plans to participate in the way it considers the wisest.

Respectfully submitted,

JAMES G. HUGHES, M.D., *Chairman*
DAVID HALE CLEMENT, M.D.
TYREE C. WYATT, M.D.
EDMUND N. JOYNER, III, M.D.
D. LESESNE SMITH, JR., M.D.
BYRON K. RUST, M.D.
JAMES B. GILLESPIE, M.D.
W. PRICE KILLINGSWORTH, M.D.
CLEMENT J. MOLONY, M.D.

Upon motion regularly made and seconded, the report of the Committee on Cooperation with American Legion was filed and endorsed in principle.

Resolution adopted at the Thirty-first Annual National Convention of the American Legion in Philadelphia, Pa., Aug. 31, 1949, introduced by the Committee on Child Welfare of the Legion.

INTRODUCTION

The children of America are its greatest asset and the Legion is interested in these children—not only the children of veterans, but all children. We must make certain that every child has sufficient food to be nourished properly daily, and a suitable environment in which to grow into healthy and useful manhood or womanhood. We will not be discouraged by any temporary obstacle that may be cast in the way. The command is forward and our efforts in conserving our Country's greatest asset will be the insurement of PEACE AND PROSPERITY for the future citizens of America.

ADVANCEMENT OF CHILD HEALTH THROUGH COMMUNITY ACTION

Resolution No. 488, from the Department of California (as amended by the Convention Child Welfare Committee):

"WHEREAS, the National Child Welfare Program of The American Legion has always been a 'whole child' program and has always been interested in child health, and

"WHEREAS, there is abundant evidence that all children are not receiving the health and medical services which they need, and

"WHEREAS, we believe the proper emphasis for improving medical care for children should come from the local community, now

"THEREFORE BE IT RESOLVED that the American Legion cooperate with the American Medical Association, the American Academy of Pediatrics and other reputable health and medical organizations and agencies in the development of a program for improved child health based on community action under community leadership."

The motion was made, seconded and carried that the Executive Board approve the resolution adopted at the Thirty-First Annual Convention of the American Legion, Aug. 31, 1949.

REPORT OF THE COMMITTEE ON COOPERATION WITH NON-MEDICAL GROUPS

The following letter, which was mailed to all state and local committee members, gives a good summary and outline of the activities of this committee:

"Dear Doctor:

"This letter is to better acquaint you with the work of this Committee and show you your important part in its program. If for any reason you cannot serve in 1950, please notify one of the National Committee.

"Each State and City Committee member is to act in an advisory capacity with the (1) P.T.A., (2) Girl and Boy Scouts, (3) Y.M.C.A., Y.W.C.A. and H.A., (4) Camp Groups and other similar lay organizations. This may include giving lay medical talks or getting some qualified person to give a talk if you can not.

"Wherever possible urge any of these organizations (especially the Camp groups) to use our Committee's printed examination cards. If desired, a rubber stamp could be used to imprint the name of the organization at the top of the card. The main purpose of the card is to try to get a fairly completed, yet standard card form for national distribution. If you have any worth while suggestions for changes, please send them in, as the card may need to be revised from time to time. These cards are being sold by Keller-Crescent Printing Company, 24 S. E. Riverside Drive, Evansville, Ind., directly to camps and schools at $1.00 for 100, $3.50 for 500 and $5.00 for 1,000 (including postage if check accompanies order).

"We are still sponsoring and urging the use of the film 'When Bobby Goes to School.' This is a film for lay use mainly and publicizes a 'check up' examination of a school child in a doctor's office. There are many copies available through Mead Johnson and Company.

"Our Committee, mainly through our member Dr. Henry Utter, is still trying to do something toward improving the National Camp situation. It was our hope to get some sort of a 'Certified Camp' program set-up to improve the general health background of most of the camps. This would have to be worked out mainly on a national basis and possibly through the American Camping Association. Many states have inadequate or even no apparent health supervision of camps. If your state is in this group maybe you can start the 'ball to rolling' to remedy the situation. The Committee would appreciate any ideas and suggestions, especially if you could get the report to any of us in time for the San Francisco meeting. If you would contact your State Health Department to find out if there are any health regulations or inspections necessary before a license can be obtained or a camp opened, the results might surprise you and be of help to the Committee.

"Dr. Cline of our Committee made a personal visit to the national headquarters of the PTA and, as a liaison member, established a much closer and more cordial relationship with this organization. Your name has been given to them for advice and help in your particular area. Their objective for the next 3 years is 'Parent Education.' The comic book question and the responsibility of the home to the school aged child will be especially emphasized and study courses arranged.

"The National Committee thanks you for your help in the past and will look forward to your continued support for all its projects in 1950."

Respectfully submitted,

JAMES C. OVERALL, M.D., *Chairman*
SHEROD M. BILLINGTON, M.D.
JOHN E. BROWN, M.D.
GERALD M. CLINE, M.D.
MARGARET M. NICHOLSON, M.D.
HENRY UTTER, M.D.

It was moved, seconded and carried that the report of the Committee on Cooperation with Non-Medical Groups be accepted with the hope that a new examination card will be presented soon.

REPORT OF THE COMMITTEE ON SCHOOL HEALTH

The evolution of school health services was quickened by several circumstances during 1949. One was the introduction of the National School Health Services Bill into the 81st Congress and its subsequent passage by the Senate in April. This legislation would authorize $35,000,000 of federal funds annually for grants to states for the development of school health services for the prevention, diagnosis and treatment of physical and mental disorders among school children. The Bill was endorsed in principle by the Executive Board of the Academy at Atlanta, April 16, 1949, although changes were recommended (1) to emphasize the importance of the family physician's services in the health supervision of children of school age and (2) to eliminate a section stipulating that states might provide treatment services for all children in this age group regardless of the parents' ability to provide such treatment themselves. When the Bill was passed in the Senate, however, this latter section was not deleted.

During the summer, in committee hearings of the House of Representatives, the Bill became entangled in discussions concerning the manner of providing health services in parochial schools and by late September had not reached the floor for a vote. Enactment in this session of Congress is considered improbable by those on the scene. It is significant that delay in passage of the School Health Services Bill was caused by disagreements about administrative details and not by opposition to the principle of expanding health services for school children.

Concurrently with favorable consideration of this nation-wide program to expand school health services, the Report of the Study of Child Health Services was published and the section of the Study which dealt with school health activities immediately achieved added significance. The findings had revealed lack of personnel trained in the health supervision of children, inadequacies in standards for school medical examinations and ill-defined objectives of school health programs in various parts of the country. It was obvious that these were gaps in health services which would not be remedied solely by authorization of funds and that they might indeed jeopardize the anticipated development of health programs in schools unless steps were taken to correct them.

On the recommendation of the Committee for the Improvement of Child Health, the Committee on School Health has worked informally with members of the American Public Health Association's Child Health Committee during the past 6 months to formulate an acceptable, up-to-date statement on the objectives, practicable scope and priorities of services which might reasonably be carried out under the proposed federal legislation. School health requires cooperative planning by educational, medical, dental and public health groups if it is to be effective. Leadership by the Academy promises to fulfill our responsibility for implementing the Study findings, but it would be fruitless, and a poor example to state and community agencies, if pediatricians should undertake the job alone. The joint planning with the American Public Health Association was instituted because that organization represents all the other professions concerned with health programs in schools and also because the Association's Committee on Child Health had recognized the underlying problems which would hold back expansion of school health and was eager for Academy support.

Our committee and the Association group were agreed that the excellent statements on school health procedure which are available have apparently missed the mark because they have not aimed at the health officers, general practitioners, pediatricians, nurses, school administrators and others who actually have the responsibility for developing and conducting these services. An authoritative statement bearing the endorsement of the professional organizations which draw membership from these groups should be most effective in influencing good school health practice.

Such a statement has been prepared and would have been presented for approval at this meeting if the School Health Services Bill had been enacted. Instead, it is the present intention to revise the recommendations by changing the original emphasis on implementation of a particular Bill to a declaration of desirable practices and standards which would apply to any situation under national, state or community sponsorship. The revised statement will be presented to the Executive Board at a later date. The American Dental Association has been exceedingly helpful in drafting recommendations for dental services in schools and has indicated an interest in being a cosignatory of the final document.

At this time, the Committee on School Health requests approval of the Executive Board to continue cooperative planning with the American Public Health Association and the American Dental Association and authorization to invite other professional organizations to share in the preparation of recom-

mendations for school health services if it becomes advisable. The assistance and concurrence of an organization of educators would, for example, increase the effectiveness of any statement on health programs for schools.

Among the barriers to satisfactory development of school health services has been conflict over the administration of school health programs. The Study disclosed that in almost half of the counties in the United States the local official education agency administers school health and in a slightly less number the official health agency is responsible. In about 10% of the counties a joint education-health administration is in operation. In view of the important role each group should play in the promotion of school health, further study of these data is recommended to determine, if possible, the local conditions which made one other plan seem more desirable. Careful study of the cooperatively administered programs is especially promising as it might contribute to solution of the frequent problem of rivalry for administrative control.

The Committee wishes to express appreciation to the Editor of "The Pediatrician and the Public" for the symposium on school health services which appeared in that column in the March, April and May issues of PEDIATRICS. The principles which the 7 contributors expressed and the issues they raised are well known to those who specialize in school health work but are not generally appreciated by physicians outside the schools. The Committee recommends thoughtful consideration of these letters by all Fellows of the Academy.

Respectfully submitted,

THOMAS E. SHAFFER, M.D., *Chairman*
ROBERT H. ALWAY, M.D.
JESSIE BIERMAN, M.D.
ALBERT D. KAISER, M.D.
HAROLD H. MITCHELL, M.D.

It was moved, seconded and carried that the report of the Committee on School Health be accepted, with the addition of the inclusion of the American Medical Association as a consultative body, in addition to the American Dental Association and the American Public Health Association.

The following reports of standing committees were presented:

REPORT OF THE COMMITTEE ON HOSPITALS AND DISPENSARIES

During the year several inquiries were addressed to the Committee requesting information and advice on plans for pediatric units in general hospitals. The physicians making these requests were referred to the publications of the Division of Hospital Facilities, U. S. Public Health Service, the U. S. Children's Bureau, and "Standards and Recommendations for Hospital Care of Newborn Infants," the report of the Committee on the Fetus and Newborn.

Early in the year the President charged the Committee with the preparation of a critique with recommendations of chapter IV—"Hospitals"—of *Child Health Services and Pediatric Education,* the report of the Committee for the Study of Child Health Services. Comments have been received from 4 of the 5 members of the Committee and discussions have been held with Dr. John P. Hubbard and Dr. Glidden L. Brooks, the Executive office of the ICH Committee. In general, this chapter covers findings as to the number and distribution of hospital facilities for children. The chief conclusion to be drawn is the fact that adequacy of hospital facilities for children, like adequacy of physicians trained in pediatrics in general, parallels the economic status of any particular section of the country. Furthermore, in like manner, there is an unbalanced distribution of adequate facilities favoring urban areas and the white population. Additional as yet unpublished data available to the ICH Committee reveal the wide variations existing in the quality of pediatric care in pediatric hospitals and in pediatric units of general hospitals.

Information now available as a result of the recently completed study of child health services is most provocative. What constitutes an adequate ratio of pediatric beds? Can a uniform ratio be established for the entire United States, or must not this ratio depend upon many factors existing in the particular region under consideration? What should be the minimum requirements for space and what is the ideal distribution of this space? This problem has been studied extensively by the Division of Hospital Facilities, U. S. Public Health Service, and the Division of Research in Child Develop-

ment, U. S. Children's Bureau. What should be the minimal educational requirements for nurse supervisors of pediatric units? How extensive can be the use of the so-called "practical nurse" or "ward-aide?" These problems are under study by many groups within the nursing profession and elsewhere. What should be the ratio of residents and interns to number of patients? What should be the minimal requirements as to laboratory, x-ray and other ancillary services?

It would seem that the time is here for close examination of the vast fund of information available on these and many other questions. The Committee therefore, recommends that the Academy now take action toward the development of standards for the care of the ill child in the hospital, and that a campaign then be inaugurated to have standards adopted in pediatric hospitals and in pediatric units of general hospitals. It is recognized that the Committee on the Fetus and Newborn has completed the first important step in this direction, in its report, "Standards and Recommendations for Hospital Care of Newborn Infants."

Respectfully submitted,

AIMES C. MCGUINNESS, M.D., *Chairman*
JOHN A. ANDERSON, M.D.
MONTGOMERY BLAIR, JR., M.D.
PETER G. DANIS, M.D.
LENDON SNEDEKER, M.D.

It was moved, seconded and carried that the report of this Committee be accepted and the Committee be instructed to bring in its recommendations, and that it further be directed to consult with the American Hospital Association and the American Medical Association's Committee on Hospitals.

REPORT OF THE COMMITTEE ON IMMUNIZATION AND THERAPEUTIC PROCEDURES FOR ACUTE INFECTIOUS DISEASES

For some time I have been working on the last published report of our Committee. As a result, much of the subject matter has been deleted, revisions have been made, and a number of additions proposed. With the changes made I have planned that each member of the Committee may review my suggestions, approve or reject them, and submit in typewritten form to me any ideas that each one may have.

At the present time, Dr. Toomey should be making a study of my revision. I have requested that each member of the Committee should not hold the revised work for a period of more than one week. If the plan is adhered to, the book should be back in my hands not later than Nov. 1. I have attempted to emphasize to our Committee members the importance of brevity, and I hope that ultimately the report will be satisfactory for presentation to the Academy. The exact date for the accomplishment of such an aim cannot be determined at this time.

If there are any further questions concerning the undertakings of our Committee, I hope you will convey them to me and I shall endeavor to supply answers.

Respectfully submitted,

ARCHIBALD L. HOYNE, M.D., *Chairman*
WILLIAM L. BRADFORD, M.D.
JOHN A. V. DAVIES, M.D.
JOHN J. MILLER, JR., M.D.
JOHN A. TOOMEY, M.D.

It was moved, seconded and carried that the report of the Committee on Immunization and Therapeutic Procedures for Acute Infectious Diseases be accepted.

The Board then discussed the Academy committees and took the following action:

The heading, "Standing Committees with State Activities," is to be changed to "Standing Committees."

The Committee on Contact Infections will be discontinued.

The Liaison Officers of the Committee on Cooperation with the American Legion were discontinued; a Committee on Cooperation with the American Legion will be appointed.

Dr. Grulee was appointed Chairman of the Committee on Pan-American Scholarships with authority to select his own committee.

The following Special Committees were discontinued: Building, Mothers' Milk Bureaus, Reorganization and Nutrition.

The following Special Committees were made Standing Committees: Budget and Tumor Registry.

The following changes are to be made in the representation to National Organizations:

American Camping Association—Chairman of Committee on Cooperation with Non-Medical Groups.

American Council on Rheumatic Fever—Chairman of Committee on Rheumatic Fever.

Children's Bureau—Dr. Clarence H. Webb.

National Conference on Family Life of the National Planning Association—no representative to be appointed.

National Foundation for Infantile Paralysis—Dr. Harold K. Faber.

Parent-Teachers Association—Chairman of Committee on Cooperation with Non-Medical Groups.

The meeting recessed for dinner at 6:15 P.M. and reconvened at 7:50 P.M., with Dr. Hubbard and Mrs. Lammie present, in addition to the members of the Board present during the day.

REPORT OF THE COMMITTEE FOR THE IMPROVEMENT OF CHILD HEALTH

This report has been prepared for submission to the Executive Board with the request that it be distributed to the membership for their information prior to the Annual Meeting at San Francisco.

It is essentially a summary of work accomplished and projected and should not be confused with a full interpretative analysis of the study findings which is described briefly in the first item below.

The report is concerned with the following matters: (1) an Interpretive Report of the Study of Child Health Services and Pediatric Education; (2) State Reports; (3) Pediatric Education; (4) Publicity and Public Relations; (5) a Program for Improved Child Health Proposed by the American Legion; (6) Finances; (7) the ICH Committee's Position in Relation to the Proposed Reorganization of the Academy.

1. An Interpretive Report of the Study.—During the past year, the ICH Committee and its staff expended much time and effort in final publication and announcement of the Study. Now that the facts are in, what do they mean? The answers will be many and cannot be given lightly. An interpretation of the findings—a study of the Study—has been one of the toughest and most important jobs given to the ICH Committee by the Executive Board. In contemplating this assignment, the Committee has been impressed first by the magnitude of the task and by the danger of careless, partial or biased misconstruction of the facts. Secondly, the Committee has felt the urgency of the matter, for already the facts revealed by the Study are being used in support of arguments both for and against compulsory health insurance. The Academy cannot delay in giving its own answer.

A preliminary draft has been prepared, separate sections of the material having been assigned as follows to individual members of the Committee: Distribution of Services, Dr. Hill; Private Practice for Children, Dr. Quillian; Undergraduate Training in Pediatrics, Dr. Platou; Graduate Training in Pediatrics, Dr. Kennedy; Public Agencies and Child Health, Dr. Wheatley; Regional Planning for Pediatric Education and Services, Dr. Kaiser; State and Community Planning, Dr. Thelander; Cost of Pediatric Service and Training, Dr. Lancaster.

As a result of extensive and detailed discussion during a 2 day meeting of the ICH Committee at Ann Arbor in September, the preliminary draft was prepared in its present form so that it may be sent to the Executive Board, Chairmen of Academy Committees, and State Chairmen to elicit their comments prior to a final draft. It is to be hoped that the State Chairmen will discuss the report with Academy members so that this document will ultimately constitute a truly representative Academy opinion.

2. State Study Reports.—As of present date, 21 state reports have been published; many others are in various stages of preparation. The appearance of state reports in increasing number has been one of the most gratifying results of the Study; these reports are based upon knowledge of local conditions and include recommendations which are being felt throughout the country in the cause of child health. One of the functions of the ICH staff has been to assist State Chairmen in the in-

terpretation of the statistical material and in the completion of their reports. Unfortunately, owing to limitation of personnel and facilities in the office of the ICH Committee, the amount of assistance which we have been able to give has been much less than some State Chairmen have requested, but also much more than the ICH Committee had envisioned.

3. Pediatric Education.—During the course of the Study, the Committee and its staff were frequently asked to advise on content, curriculum and technic of teaching, with specific reference to the findings of the Study. Many department heads requested further conferences to provide opportunity for exchange of opinion in regard to pediatric education. Prior to the analysis of the data, satisfactory answers to many important questions could not be made. Now, however, many of these questions can be answered.

Regional meetings are now being undertaken in order that pediatric department heads, District Chairmen and State Chairmen may meet together in small, informal groups to discuss the problems of pediatric education. The first such meeting has been scheduled for Oct. 26 in Detroit and the second meeting will be held in San Francisco on Nov. 17. Other meetings will be held during the ensuing months in order to cover all medical schools.

Regionalization and decentralization of pediatric education and services continues to be one of the predominant projects of the Committee. A compilation of the experiences, successes and failures of plans already in existence or contemplated are already proving a valuable guide to further planning. In accordance with approval given by the Executive Board, the staff of the ICH Committee has agreed to help the District III Committee in establishing a regional program. It is agreed by all that this project should be self supporting. Accordingly, a duly appointed local committee is now undertaking to raise the necessary funds from local sources.

A roster of pediatric residencies has been set up and maintained. Help has been given to schools seeking residents and to residents looking for available openings.

4. Reports for Lay Consumption.—Our pamphlet, "The Road Ahead for Better Child Health" is familiar to you. It was 9 months in preparation, in which time photostatic copies were prepared for review and comment by the Committee and Executive Board. Nearly 8,000 copies have been distributed and the demand continues to grow. It should be noted that the production of this pamphlet cost $3,500 for an initial printing of 5,000 and $800 for a second printing of 5,000—a cost which is approximately one third that of similar pamphlets prepared by other organizations.

Ever since the Academy Committee on Publicity and Public Relations was appointed under the Chairmanship of Dr. Barba, our executive staff has been placed at their service. The announcement of the Academy Report at the Dinner Meeting in New York on April 2, together with the news items which appeared throughout the country, was part of the service which was rendered to the Publicity Committee. You are also familiar with the Publicity Bulletin mailed to all Academy members with covering letters from Dr. Barba and Mr. Hiller. Incidentally, this Bulletin resulted in a great increase in the requests for additional copies of "The Road Ahead."

It is with sincere regret that we must report that Mr. Hiller's services with the ICH Committee terminated during the past summer, the only reason being that the funds available for the ICH Committee were insufficient to continue his salary.

5. A Program for Improved Child Health Proposed by the American Legion.—At the time of the Annual Convention of the American Legion in August, there arose further evidence of the increasing interest and support of lay groups in the prevention of disease and improvement of health for infants and children. A well defined program for improved child health was advanced by the Legion's Committee on Child Welfare. This action, which has its roots in more than 20 years of a liaison relationship between the Academy and the Legion, had recent stimulation from the Committee on Cooperation with the American Legion. At the request of Dr. Hughes, Chairman of this Committee, the staff of the ICH Committee has met with officials of the Legion and subsequently with officials of the American Medical Association for further development of the program.

A further description of this program will be found in the Report to the Executive Board from the Liaison Committee.

6. Finances.—There is, as of Sept. 1, 1949, approximately $34,000 on hand or pledged to the credit of the ICH Committee for the remainder of this year and next. Reference should be made to the Treasurer's Report for an accounting of these funds and all expenditures of this Committee, since all disbursements are made from the Treasurer's office.

It is estimated that these funds are sufficient to carry on the work of the Committee, exclusive

of the Director's salary, until the end of 1950—16 months at approximately $28,000 per annum for the activities of the Committee. At the meeting in Ann Arbor (Sept. 18 and 19) the ICH Committee requested the Executive Board to assume responsibility for supplying the salary of the Committee Director as of Nov. 1, 1949.

7. The ICH Committee's Position in Relation to Reorganization.—It has been increasingly apparent that unavoidable confusion and difficulties in the management of Academy affairs have resulted from the wide geographic separation of the Secretary-Treasurer's office in Evanston and the ICH office in Philadelphia. Accordingly, at the Ann Arbor meeting it was also recommended that the Committee for the Improvement of Child Health, as now constituted, be dissolved at the discretion of the Executive Board, but that the functions which have been assigned to it be absorbed into any plan of reorganization which the Board may adopt.

Respectfully submitted,

COMMITTEE FOR THE IMPROVEMENT OF CHILD HEALTH

It was moved, seconded, and carried that the report of the Committee on Improvement of Child Health be accepted.

It was moved, seconded and carried that the Interpretive Report of the Study of Child Health Services and Pediatric Education be published as an Academy Publication, the exact method of publication to be determined by the Publication Committee.

The meeting recessed at 9:35 P.M. to reconvene Saturday, Nov. 12, at 9:00 A.M.

Saturday, Nov. 12

The meeting was called to order at 9:15 A.M. by the President. The members present on Friday, with the addition of Drs. Felix Hurtado, Roger L. J. Kennedy, Preston McLendon and Frank Lancaster, attended this meeting, with Drs. Hubbard, Veeder, Wall and Baty present during a part of the proceedings.

The report of the Budget Committee for the ICH Committee was presented and discussed. Action was postponed.

The report of the Committee on Reorganization was presented and discussed.

After further discussion of the report of the Committee on Reorganization, motion was made, seconded and carried that the report be accepted.

The Board then went into Executive Session.

The Executive Board in Executive Session considered the question: Should the ICH committee be continued at least until the proposed reorganization is put into effect?

It was the considered opinion that all previous developments and current discussions obligate the Academy to answer this question in the affirmative. In addition, an abrupt discontinuance of the work of this committee and its staff would produce a dangerous hiatus in the present progressive program of the Academy.

The recommendation of the Budget Committee for the ICH Committee, which was accepted by the Board, was that the American Academy of Pediatrics assume the obligation of underwriting the expense of the ICH Committee to the extent of the Director's salary during the period between now and the next annual meeting in October 1950.

1. During this time, no new projects are to be initiated by the ICH Committee without first being cleared through the Board.

2. There shall be no additional solicitation of funds by the ICH Committee.

3. There shall be no budgetary increases. The total expense shall not exceed the budget of $25,650.00.

4. By the time of the next annual meeting, the ICH Committee as presently constituted will be dissolved and its functions absorbed by the central organization.

5. Any grants received by the Academy for the ICH Committee function during this time will correspondingly reduce the $15,000.00 commitment by the Academy.

The motion was made, seconded and carried that the Executive Board approve the report of the Reorganization Committee and recommend it to the State Chairmen and the assembled membership at the San Francisco meeting for their information, and that it be submitted to the entire membership by mail vote for final action.

The Executive Session adjourned and the Board reconvened in regular session.

REPORT OF THE PUBLICATION COMMITTEE

Since our report to you last year, PEDIATRICS has made great strides and certainly now justifies the action of the Academy in taking over its publication. At the end of our first volume of 6 issues, we showed a loss of several thousand dollars. In every department the budget had been exceeded and we explained this on the basis of the unforeseen expenses in the process of organizing and launching a new project, the details of which were not all too well known to us.

By Dec. 31, 1948, at the end of volume 2, we found ourselves out of the red, and while only slightly over to the credit side, the future gave promise that was much more encouraging and it was most gratifying to find that in the short space of a year we had come of age and were out on our own.

With the completion of volume 3 on June 30, this year, we showed a definite increase in receipts over expenditures, although again unforeseen events came in to cause us to exceed our budget as submitted. In this period the editorial offices were moved from St. Louis to Chicago where Dr. McCulloch had to set up new quarters, employ new help and practically go through the process of reorganization. This he did with no perceptible irregularity in office routine or publication schedule and operation has continued as smooth as could be hoped for. Dr. McCulloch has taken over the position as head of La Rabida Jackson Park Sanitarium and all communications should be addressed to him there.

All revenues have shown an increase over the estimates on our budget and this accounts for the respectable profit shown in spite of the extra expenses entailed. The subscription list has increased rapidly; early this year it exceeded 5,000 and has continued to build up since that time. Advertising has exceeded the budgeted figure and we now run approximately 50 pages per issue. Reprints, while never a big item, have shown a fair profit for the entire time and we now look forward with much more assurance to obtaining the goal which we have set for ourselves in these respective departments.

It is with much pleasure that the Publication Committee brings you this report on our journal.

Respectfully submitted,

FRANK H. LANCASTER, M.D., *Chairman*
ROGER L. J. KENNEDY, M.D.
OLIVER L. STRINGFIELD, M.D.

Ex Officio, HUGH MCCULLOCH, M.D.
EDGAR E. MARTMER, M.D.

It was moved, seconded and carried that the report of the Publication Committee be accepted.

REPORT OF DISTRICT IX

During the past year there has been intensive activity in District IX which has met with great enthusiasm. The number of members of this District is now over 200 and all the Latin American countries are included except Haiti and Paraguay, since a branch has recently been organized in Bolivia.

The Cuban branch held a meeting at Miami Beach, Fla., as the guests of the U.S. members in that region and especially with the kind cooperation of Dr. Warren Quillian.

As Chairman of District IX, I have attended almost all meetings of the Executive Board and I am particularly interested in the projected reorganization of the Academy. All members of District IX wish to express their deep appreciation of the wonderful job done by Dr. Clifford G. Grulee as Secretary-Treasurer of the Academy. For that reason we present, for the consideration of the Executive Board, a motion proposing the nomination of Dr. Clifford G. Grulee as Honorary Secretary of the Academy for life and proposing that when Dr. Grulee retires he be accorded a life pension because of his work for the Academy.

District IX wishes to propose that there be a special Assistant Secretary for the handling of Latin American affairs, since they feel it is the best way to develop the Latin section. They wish to present this proposition to the Executive Board.

I want to take this opportunity to present my cordial salutations and greetings to all the Executive Board for the kindness extended to me during the term served by me as Chairman, and to request that my successor receive the same cooperation.

Under the presidency of Dr. Felix Hurtado, Chairman of District IX, and with the assistance of

Dr. Federico Gomez, Alternate Chairman, Dr. Jesús Lozoya Solís, Local Chairman of Mexico, and Dr. Enrique Galan, Local Secretary of the Cuban Republic, there were present the following Latin American representatives of the different countries constituting District IX of the American Academy of Pediatrics:

Argentina—Dr. Roldofo Kreutzer; Brasil—Dr. Leonel Gonzaga; Chile—Dr. Aníbal Ariztía A.; Colombia—Dr. Camacho Gamba; Cuba—Dr. Emilio Soto Pradera; Dominican Republic—Dr. Jaime Jorge; Guatemala—Dr. Manuel Girón; Mexico—Dr. Jesús Lozoya Solís, *Local Chairman,* Dr. Antonio Prado Vertiz, *Secretary;* Nicaragua—Dr. Germán Castillo; Panama—Dr. Leopoldo Benedetti; Peru—Dr. Carlos Krumdieck; Uruguay—Dr. María Luisa Saldún de Rodriguez; Salvador—Dr. Ranulfo Castro; Venezuela—Dr. Pastor Oropeza.

There were present over three fourths of the Latin American members of District IX.

The business meeting was opened and the election of a new Chairman for District IX proceeded according to the rules and regulations of the Academy.

The following recommendations were made: Dr. Federico Gomez, Mexico—Chairman; Dr. Pastor Oropeza, Venezuela—Alternate; Dr. Carlos Krumdieck, Peru—Alternate; Dr. Aníbal Ariztía A., Chile—Alternate.

A proposition was made for a fourth Alternate Chairman to care for the Central American business of the Academy; Dr. German Castillo was recommended for such new position.

The city of Montevideo, Uruguay, was selected as the place for the celebration of the Third Pan-American Pediatric Congress or Third Biennial Meeting of District IX of the American Academy of Pediatrics. The Congress will be held in November 1951 and it will not last longer than 4 days. Dr. Conrado Pelfort, Local Chairman of Uruguay, was appointed President of the Organizing Committee.

It is the feeling of the members of District IX that the term of Chairman of District IX should be limited to no longer than 2 years. The reason for this limitation of term is that the only opportunity for a meeting of the whole membership of District IX is the Pan-American Pediatric Congress, which, as is well known, is an event called every 2 years.

We recommend to the Executive Board of the Academy that due consideration be given to the economic situation in many Latin American countries, where it is extremely difficult to exchange current money into American dollars. Therefore, some resolution must be adopted for avoiding the dropping of membership in the Latin American countries.

We request from the Executive Board the re-establishment of the Latin American scholarships.

This meeting was held in the city of Mexico on the 4th of November, 1949.

Respectfully submitted,

FELIX HURTADO, M.D., *Chairman*

It was moved, seconded and carried that the report of District IX be accepted, including the following recommendations:

1. That there be a Fourth Alternate Chairman of District IX to represent the Central American countries.

2. That the term of the District Chairman of District IX be 2 years, since the only opportunity for the entire District IX to meet is at the Pan-American Pediatric Congress, which is held biennially.

The following elections in District IX were approved: Dr. Federico Gomez, Mexico—Chairman; Dr. Pastor Oropeza, Venezuela—Alternate; Dr. Carlos Krumdieck, Peru—Alternate; Dr. Aníbal Ariztía A., Chile—Alternate.

If the Fourth Alternate Chairman is approved, it was the recommendation of District IX that Dr. Germán Castillo of Nicaragua serve in that office.

It was moved, seconded and carried that a formal vote of thanks for his excellent work be given Dr. Hurtado by the Executive Board.

It was moved, seconded and carried that the Secretary and the President extend officially the thanks and appreciation of the Academy for their hospitality in the recent Pan-American meeting.

It was moved, seconded and carried that Dr. Grulee be authorized to look into the matter of District IX members impounding their dues.

It was moved, seconded and carried that Dr. Grulee be authorized to renew the lease of the Evanston office for a period of one year from May 1950.

It was moved, seconded and carried that the $1,000 loaned to Connecticut and now repaid be put into the "general fund."

It was moved, seconded and carried that Dr. Grulee be empowered to solicit funds for the Pan-American Scholarships.

REPORT OF THE COMMITTEE ON PAN-AMERICAN SCHOLARSHIPS

At this time it might be well to take stock of our accomplishments in the past and see what the future has in store for us.

During the period following the war it was impossible to find places for Pan-American scholars, so that since 1945 no foreign students have been granted scholarships.

In the years before and during the war, there have been 29 Academy scholarships sponsored by the Kellogg Foundation, 5 sponsored by the M & R Dietetic Laboratories, 3 sponsored by Mead Johnson, 2 sponsored by Quaker Oats, and 1 each by Proctor and Gamble and the Abbott Laboratories. There is a total of 41 scholarships, which have been enjoyed by young men who are now back in their home countries, many of them actively teaching in their local medical schools.

In addition to the 29 scholarships for foreign students that were granted by the Kellogg Foundation, it, together with the Infant's Hospital of Mexico City, has granted one scholarship to a resident of the USA for a year's study in the Infant's Hospital of Mexico City. Dr. Jack L. Grieg was the first scholar to occupy this position. He served for the period from July 6, 1947, to June 7, 1948. I would like to quote just a few sentences from a report that he made to the Kellogg Foundation.

"I can say without fear of being mistaken that the opportunities at the Hospital Infantil would compare favorably with the large university teaching hospitals in the USA and exceed many of the hospitals approved for pediatric training. Beyond this, there is the opportunity to view American medicine from without, learn other attitudes and approaches, and to grasp the tremendous force American research and writings has on other countries."

Now as to the future: We have communicated with the various pediatric departments of medical schools and children's hospitals regarding opportunities for foreign students at the present time. In answer we have received 24 favorable replies out of 38 inquiries so it would appear that the postwar overload has subsided to the extent that numerous places are now available.

With regard to available scholarships, the outlook is not so favorable. The Kellogg Foundation is engaging in a postgraduate training program for the Americas that will make available only an occasional scholarship for pediatrics. Mead Johnson also has started an educational program that includes only those of a higher academic rank. Other available sources are being investigated at the present time.

Institutions offering opportunities for foreign students:

Harvard University
Southern California University
Columbia University
Long Island—Jewish Hospital of Brooklyn
University of Michigan
Mayo Foundation
New York University—Bellevue Center
Winnipeg University—Children's Hospital
Tulane University of Louisiana
Cornell University
Baylor University
Louisiana University
University of California
Western Reserve University
University of Illinois
University of Iowa
University of Kansas
University of Rochester
University of Texas
Johns Hopkins
University of Pennsylvania
University of Buffalo

Respectfully submitted,

HENRY F. HELMHOLZ, M.D., *Chairman*
SAMUEL Z. LEVINE, M.D.
DONOVAN J. MCCUNE, M.D.
FRANCIS SCOTT SMYTH, M.D.

No action was taken on this report.

REPORT OF THE COMMITTEE ON PEDIATRIC AWARDS

Borden Award—Dr. Alfred Washburn
Mead Johnson Awards—Dr. Nathan Talbot
Dr. Henry Barnett

No action was taken on this report.

Dr. Grulee was asked to bring in a report at the June meeting concerning changes in the system of pediatric awards.

REPORT OF THE SECTION ON MENTAL GROWTH AND DEVELOPMENT (COMMITTEE ON MENTAL HEALTH)

One meeting of the steering committee of the Section on Mental Growth and Development (Committee on Mental Health) has been held and much discussion has gone on by mail between its members. Organization of the Section, aims, functions and standards of eligibility for membership were discussed. The following suggestions are made to the Executive Board of the American Academy of Pediatrics:

1. That the Section act as an educational force for the pediatric profession, promulgating interest and activity in the fields of mental growth and development and mental hygiene and in the psychologic implications of pediatric care and child-rearing through serving as a discussion group.

2. That Section membership be made up of Academy members with interest in mental hygiene and in the psychologic aspects of pediatrics, including particularly those members with special training and experience in medical psychology or its equivalent. (See list of nominations for memberships.)

3. That the Section should not serve as an agency for establishing a subspecialty of "pediatric psychiatry," nor in fostering among pediatricians training which would encourage the practice of child psychiatry unless these individuals had also received adequate training in psychiatry.

4. That meetings of the Section be held at least annually at the time and place of the annual meeting of the Academy, but that members of the Section may organize regional or local meetings at other times.

5. That the Section be responsible for assisting the officers of the Academy in selecting leaders of seminars and panel-group meetings of the Academy at annual and regional meetings, for assisting in any other way in furthering the education and training of pediatricians, and for stimulating the production of papers and other education material for publication in the journal PEDIATRICS.

6. That membership of the Section be kept small, particularly at the beginning, probably never numbering a total membership of more than 40. That this be done in order to encourage group discussion which is free, yet organized, and at a stimulating level.

The steering committee, in considering membership in the Section, for the present proceeded by combing the Academy membership, each member of the committee nominating those individuals whom he believed satisfied in general the criteria mentioned above. The nominations were then pooled and the total submitted to each member for vote. The votes were collected and counted by an impartial person who was not a member of the steering committee. As a result of this poll by the steering committee the following members are nominated to the Executive Board for election to charter membership:

John C. Montgomery
C. A. Aldrich
Ann Martin
Grover Powers
James M. Baty
Henry H. Work, Jr.
Leona Baumgartner
Percy Hall Jennings
Sherman Little
Henry G. Poncher
George H. Schade
Samuel R. Berenberg
Charles Bradley
Maurice W. Laufer
Paul W. Beaven
Marjorie F. Murray
Otto A. Faust
William A. Schonfeld

Although the name of the Section has tentatively been given as "Section on Mental Growth and Development" (Committee on Mental Health), there have been other suggestions. Such suggestions as "Section on Behavior Problems of Children," "Section on Personality and Development Problems,"

"Section on Mental Aspects of Pediatrics," "Section on Psychological Aspects of Pediatrics," and "Section on Mental Hygiene in Pediatrics" have been received. For the time being, the steering committee suggests retaining the name "Section on Mental Growth and Development (Committee on Mental Health)."

The members of the steering committee of the Section were appointed to office for varying lengths of time by the President of the Academy. Two appointments were for 1 year, 2 for 2 years and 2 for 3 years. Provision was made for the Chairman to serve for a period of 3 years, with re-election for 1 more term permitted, but both the chairmanship and membership on the steering committee were to be revolving. The appointment of 2 members of the steering committee to replace 2 whose tenure was for 1 year is therefore suggested at this time to the Executive Board and the President.

Respectfully submitted,

MILTON J. E. SENN, M.D., *Chairman*
KATHERINE BAIN, M.D.
ARNOLD GESELL, M.D.
WILLIAM LANGFORD, M.D.
BENJAMIN SPOCK, M.D.
ERNEST WOLFF, M.D.

It was moved, seconded and carried that the report of the Section on Mental Growth and Development (Committee on Mental Health) be accepted and approved.

The following reports of Special Committees were presented.

REPORT OF THE COMMITTEE ON GEOGRAPHICAL DISTRIBUTION OF PEDIATRICIANS

The various surveys, made upon request, have covered almost all the states. Most of the requests were for surveys of Oregon, Washington, Florida, Georgia, Alabama, Mississippi, Texas and Louisiana.

To show how favorably these surveys are being received, may I quote from recent correspondence: "Many thanks for your very complete reply to my inquiries. . . . Again many thanks." "Thank you very much for your very complete survey of the state of Florida. It was of great help." "This will be a great help in my search for a place to practice pediatrics."

Respectfully submitted,

OTTO L. GOEHLE, M.D., *Chairman*

It was moved, seconded and carried that the report of the Committee on Geographical Distribution of Pediatricians be approved and accepted.

REPORT OF THE COMMITTEE ON CARE OF EUROPEAN CHILDREN

From March 16 to July 19, 1949, 253 displaced children have been examined in various Reception Centers in New York City. The nationalities follow:

Austrian	2	Polish-Ukrainian	9
Estonian	6	Rumanian	2
German	3	Ukrainian	12
Hungarian	1	White Russian	7
Latvian	138	Yugoslavian	30
Lithuanian	23	Stateless	9
Polish	11		

I wish again to emphasize that your committee depends upon the voluntary support of physicians who are authorities in their special fields. These physicians are not affiliated with the American Academy of Pediatrics. Their services are given freely and in a fine spirit of cooperation. On occasion when hospitalization has been required, patients have been admitted to the New York Hospital.

Routine examinations are carried out in the Reception Center by a resident physician with the assistance of a group of pediatricians, usually Academy members. The United States Committee for the Care of European Children submits all medical problems to your Committee and our relationship has been cordial and mutually helpful.

Respectfully submitted,

CARL H. SMITH, M.D., *Chairman*
ROBERT A. BIER, M.D.
CARL H. LAWS, M.D.
WALTER LEVY, M.D.
RUSTIN MCINTOSH, M.D.
DOUGLAS D. MARTIN, M.D.
LENDON SNEDEKER, M.D.
PHILIP M. STIMSON, M.D.
JOSEPH STOKES, JR., M.D.

It was moved, seconded and carried that the report of the Committee on Care of European Children be accepted with congratulations and thanks for the Committee's effort.

REPORT OF THE AMERICAN BOARD OF PEDIATRICS

November 1948—December 1949

The American Board of Pediatrics has held 4 examination sessions—Atlantic City, N.J., in November, St. Louis, Mo., in February, Baltimore, Md., in May, and Cleveland, Ohio, in September. A total of 239 candidates were examined, of whom 195 were certified and 44 failed. There are 2 more sessions scheduled for this year, one at Brooklyn, N.Y., on Oct. 21, 22 and 23, 1949, and one at Chicago, Ill., on Dec. 9, 10 and 11, 1949. It is expected to examine 128 candidates at the 2 sessions.

Lists for the examinations scheduled for the year 1950 have been filled for some time. Exact details concerning these will be sent you at a later date.

Respectfully submitted,

LEE FORREST HILL, M.D.
HUGH MCCULLOCH, M.D.
A. WILMOT JACOBSEN, M.D.
JOHN MCK. MITCHELL, M.D., *Executive Secretary*

It was moved, seconded and carried that the report of the American Board of Pediatrics be accepted.

REPORT OF THE COMMITTEE ON SURGICAL AFFILIATES

The Section on Surgery at present consists of 19 members, 6 of whom were members of the Academy before the formation of this Section, the remaining 13 being members who were accepted as Surgical Affiliates at the meeting in Atlantic City.

Six additional applications have been received. They are as follows: Henry W. Hudson, Jr., Dudley E. Ross, T. W. Mustard, Elliott Hurwitt, E. E. Arnheim, Robert R. White. The Committee also has on file the names of 34 surgeons who are particularly interested in the surgery of infants and children but who are doing less than the 90% recommended by the Board.

It will be recalled that the Board also recommended that the Section consist of not more than 20 members for the present. Several of the applicants are highly desirable and it is recommended that this limitation be raised.

Application blanks for Affiliates have been devised and are available. The procedure to be followed in processing these applications has been worked out.

The minutes of the organizational meeting at Atlantic City have been filed with the Secretary's office. An outline of the aims and objects of the Section has been formulated and was presented to the Board at the June meeting.

A request has been received from Dr. Fontana, Professor of Children's Surgery in Montevideo, for reprints and articles pertaining to the practice and teaching of children's surgery for study in connection with a book on pediatric surgery which he is writing for use in the Latin American countries.

A request for information regarding placing a Fellow under the Mead Johnson Fellowship for Pediatric Research for the Latin American countries was received, and the Fellow was satisfactorily placed.

It is apparent that there is a steadily increasing interest in the surgery of infancy and childhood throughout the United States and Canada, and that an interest is well under way in South America, and it would seem that the Academy and its Surgical Section may well act as a clearing house for information, both national and international, for questions relating to pediatric surgery. The Academy is in a position of leadership in this development.

The term of office of 2 members of this Committee—Dr. Henry Swan, Jr., and Dr. William E. Ladd—will terminate at the San Francisco meeting. According to the Board's recommendation, they are eligible for reappointment for one 3 year period. Their reappointment or that of their successors is on the agenda for the next meeting of the Committee and will be transmitted for the consideration of the Board.

Respectfully submitted,

HERBERT E. COE, M.D., *Chairman*
OSWALD S. WYATT, M.D.
JESÚS LOZOYA SOLÍS, M.D.
ROBERT E. GROSS, M.D.
WILLIAM E. LADD, M.D.
HENRY SWAN, JR., M.D.

It was moved, seconded and carried that the report of the Committee on Surgical Affiliates be accepted.

It was moved, seconded and carried that the limitation on the number of Affiliates in Surgery be determined by the members of the Steering Committee of the Section.

Since the work of Dr. Preston A. McLendon, as Liaison Officer to the American Hospital Association, is finished, it was decided to drop that liaison office.

REPORT OF THE COMMITTEE TO REPRESENT THE ACADEMY IN MEETING WITH THE LIAISON COMMITTEE OF THE AMERICAN MEDICAL ASSOCIATION

Cordial and effective cooperation between this committee and the similar committee of the AMA has continued during the interval since the report made June 26.

Since the last report the following events have occurred:

Dr. Walter B. Martin, Chairman of the AMA committee was informed that the Executive Board deeply appreciated his effective cooperation in the passage of the resolution in which the AMA advocated the state societies' working with the Academy. He was sent a copy of the letter on this subject we had sent to each of our members. Dr. Martin was glad to request that a similar letter be sent from the AMA to the secretaries of each of the state medical societies and a request that they call the attention of the county organizations to this resolution.

There has been a certain amount of over-lap in the function of this committee and that of the Committee on Public Relations. Dr. Martin has been informed of all actions of the latter committee involving the AMA as described in its report and has approved those actions and expressed willingness to help in any way possible. He suggested a joint meeting of the 2 liaison committees at the time of the Dec. 6-9 meeting of the AMA. This committee feels that a great deal has been accomplished and that the future holds promise of more active cooperation with the AMA.

Respectfully submitted,

PHILIP S. BARBA, M.D., *Chairman*
WILLIAM WESTON, JR., M.D.
WOODRUFF L. CRAWFORD, M.D.

It was moved, seconded and carried that the report of the Committee to Represent the Academy in Meeting with the Liaison Committee of the AMA be accepted.

A letter of gratitude for his work for the Academy, signed by all members of the Executive Board, was sent to Mr. Eldredge Hiller.

It will be suggested to Dr. Hugh McCulloch that each monthly issue of PEDIATRICS contain a page to be written by a different member of the Executive Board; first, the President; second, the President-Elect; followed by each of the 9 District Chairmen.

REPORT OF THE COMMITTEE ON PUBLICITY AND PUBLIC RELATIONS

By the nature of its title, the functions of this committee are 2 fold and this report will take up the 2 phases in separate sections. Only the period since the last report will be considered.

Publicity

Actions Accomplished:

I. A letter describing the passage of the AMA resolution on cooperation with the American Academy of Pediatrics in child care programs has been sent to each of the Fellows over the signature of the State Chairman of the respective member.

II. A leaflet containing an abstract of Mr. Hiller's report to this committee and excerpts from the letters from the various types of organizations requesting more copies of the pamphlet "The Road Ahead . . ." was sent to all the members with a covering letter from this committee urging them to note the interest in Academy activities. Thanks to the efforts of Mr. Hiller, the total cost of this leaflet was kept down to $208.15.

We have received letters from Fellows all over the country asking for more copies. When these were sent out, they were accompanied by a letter suggesting that the extra copies be used to interest the local community groups in the work of the Academy and child care programs.

Actions Considered:

I. The Lawrence H. Selz Organization submitted to Dr. Grulee a program suggesting a national advertising type of set-up. This would consist of periodic releases to newspapers and journals of material to be used for news articles, to be worked up by the paper's editors when needed, and also, arrangements for radio time on scripts prepared by the Academy and regular coverage of the meetings as in the past. This is a brief summary only. The plan would cost $10,000.00 a year.

In the opinion of a majority of this committee, such a plan would not answer the needs for the moment. It is aimed at the lay public; it is a mechanized commercial type; it would require careful and constant supervision of releases; it has nothing to do with the publicity among Academy members which is now very important and there would be added costs for the latter feature and the supervision and script preparation.

It is our opinion that the publicity should be under the eye of a full-time staff member who could have close relations with a national concern or with the same outlets used by national concerns. Such a person should have the Academy as his or her prime interest and should also be thoroughly indoctrinated in medical ethics and public relations aspects of the problem. In this respect, we regret the loss of Mr. Hiller. While he was in the employ of the ICH Committee, he was sincerely and enthusiastically devoted to the cause of the Academy. (An article of his appears in *The Child,* June 1949, vol. 13, no. 12, on the subject of the Academy's report on the Health Survey.) His advice and apparently unlimited capacity for work has been invaluable to this committee during the past year.

II. We spoke informally at the last meeting of the Executive Board of the possibility of an annual or semiannual report which would include all the minutes of the Academy and Board meetings and of the various committees instead of having them come out piecemeal in the official journal. The expense of such a project made it seem impossible at the moment.

We are now considering the possibility of a news letter to be sent to the membership as often as possible. This would have abstracts or comments on the work of the different committees; personal notes on the activities of various Fellows and notes on the activities of other organizations dealing with child health. It might be financed by advertisements.

Public Relations

Actions Accomplished:

I. Due to the activity of Dr. James G. Hughes, Liaison Officer to the American Legion, the Academy was well represented at a meeting of the Executive Committee of the Legion's National Child

Welfare Committee. At this meeting, there were representatives from the AMA to discuss the Legion program. Dr. Hughes will report on that phase of the meeting. As a result of this association and subsequent conversations between Dr. Hubbard of the ICH Committee and Mr. Thomas Hendricks, Executive Secretary of the AMA Council on Medical Service, our committee approached Dr. McVay, Chairman of the Council, and they are inviting the Academy to send representatives to the Correlating Committee on Maternal and Child Health which will work under the Council.

II. At the request of the Public Relations Committee, Dr. Hubbard and Dr. Grulee conferred with Dr. Lull of the AMA on the subject of our close cooperation on any program the Legion may be stimulated to institute and on other problems. At that meeting, Dr. Lull agreed to notify State and County groups of the AMA of the proposed Legion program and the desired cooperation between the Academy and the AMA. As a result of this, our State Chairmen should find a ready approach to the other groups.

There is also a probability that there will be closer cooperation between the AMA Council on Education and Hospitals and our own Committee on Medical Education.

These developments have appeared in the last few weeks and we are reporting them while still in the process of accomplishment. We hope there will be definite developments by the time of the November meeting.

We wish to express our appreciation to Dr. James G. Hughes, Dr. John P. Hubbard and Dr. Clifford G. Grulee for noticing and following up these openings.

Recommendations

1. A definite budget for Publicity and Public Relations, to be made as large as possible with the state of the Academy finances as they are.
2. A news letter to the membership at frequent intervals. This to carry enough personals to make it catch the eye, committee reports to make it valuable and advertisements to make it possible.
3. If the news letter is impossible, the news and notes page of PEDIATRICS should be enlarged and enhanced to carry the same effect.
4. All Academy members should be urged to be alert for publicity and public relations material; this committee will be very glad to have the advantage of their help.
5. That no definite contract for full-time publicity be undertaken until further possibilities have been studied. However, the Budget Committee should carry an item for such expense if it becomes possible during the year.
6. State Chairmen and Liaison officers should be advised of these developments and urged to foster local Legion relations and programs. The resolution is satisfactory but the program will not go into effect without continued stimulation.

Respectfully submitted,

PHILIP S. BARBA, M.D., *Chairman*
OLIVER L. STRINGFIELD, M.D.
EDWARD A. WISHROPP, M.D.

It was moved, seconded and carried that the report of the Committee on Publicity and Public Relations be accepted.

An amendment to the By-Laws requested by Dr. William C. Black was considered by the Executive Board, and the motion was made, seconded and carried that it be submitted to the Business Meeting with a recommendation that it be rejected.

REPORTS OF REPRESENTATIVES TO NATIONAL ORGANIZATIONS

American Camping Association

In making a report as Liaison Officer of the American Camping Association, I would state that I have in the past year made several contacts with the Camping Association with rather poor results. I offered them the medical services of the Academy in an advisory capacity.

In November at the Atlantic City meeting, the Committee for Cooperation with Non-Medical Groups formulated a plan which we thought would appeal to the camping group. We asked them to appoint members from each section of the American Camping Association, which sections cor-

respond rather closely to the Academy districts, to meet with members of the Academy to discuss matters of health and safety in summer camps for children.

I personally presented this plan to the President and Executive Board. Some enthusiasm was expressed for the plan which was to be presented to the Camping Association. This was the beginning and the end, for I have had no communication from them.

My own viewpoint in the matter, to explain their lack of cooperation, lies in the fact that when the camping business is good, as it was until 1949, this group is entirely sufficient unto itself. The financial end is the most important. Much was accomplished in the Academy contacts with the Association before the war, but little since. Later, with a financial recession, they may be again asking for help.

I wish to thank the Executive Board of the Academy for asking me to serve in the capacity of Liaison Officer but, in view of my poor results, I think that some younger member of the Academy might accomplish more than I have.

Respectfully submitted,

HENRY E. UTTER, M.D., *Liaison Officer*

No action was taken on this report.

American Council on Rheumatic Fever

The annual meeting of the American Council on Rheumatic Fever of the American Heart Association, Inc., was held in Atlantic City, N.J., on June 3, 1949. Mr. Lawrence J. Linck presided. The 2 representatives of the American Academy of Pediatrics on the Council, Dr. Hugh McCulloch and Dr. Alexander T. Martin, were present.

Dr. Ann G. Kuttner reported for the Research Study Committee and said that of 5 applications for grants-in-aid, none were considered worthy of being recommended for approval. She reported on the Research Committee's consideration of heredity studies in rheumatic fever, and the morbidity factor of this disease in twins from the standpoint of human genetics.

It was voted that a letter of thanks be sent to the Advisory Committee of the American Legion for the valuable aid given by the Legion to the Council's work, also to the Legion itself and the Legion Auxiliary.

It was voted that a contribution of $1000 be made from Council Funds to the Commission on Chronic Illness, and that a hearty endorsement and approval be sent.

Dr. George M. Wheatley reported as Chairman of the Committee on Community Rheumatic Fever Programs. It was felt that it would not be wise at this time to proceed too rapidly with the plans for evaluating rheumatic fever programs and that it would not seem wise to spend large sums of money for this purpose.

Miss Dora Young reported on the Directory of Facilities for Care.

The 2 American Legion Fellows, Dr. Samuel T. Schlamowitz and Dr. Joseph E. Warren, reported on the studies they have been carrying out as Fellows of the American Legion.

Dr. Bernice Wedum reported on behalf of the American School Health Association, and stated that because of the recent publicity on heart disease, there were an increasing number of false diagnoses being made and also that an increasing number of congenital cardiacs are being screened out in the rheumatic heart disease clinics. It was suggested that a separate section on Congenital Heart Disease be set up in the American Heart Association to take care of this group of some estimated 60,000 children. The report was referred to the Committee on Standards and Criteria for Programs of Care for further consideration and study.

The next Annual Meeting will take place at the time of the Annual Meeting of the American Heart Association.

Respectfully submitted,

ALEXANDER T. MARTIN, M.D., *Liaison Officer*

It was moved, seconded and carried that this report be accepted.

National Commission on Children and Youth

During the spring, a meeting of the National Commission on Children and Youth was held in Washington, D.C., for the purpose of planning for the 1950 White House Conference. Dr. Preston

McLendon of Washington graciously attended the sessions as the Academy representative as my substitute.

Since publicity for the forthcoming Conference will appear abundantly from other sources, it need not be repeated here.

Respectfully submitted,

LEE FORREST HILL, M.D., *Liaison Officer*

No action was taken on this report.

National Maternal and Child Health Council

The International and Fourth American Congress on Obstetrics and Gynecology will be held in the Hotel Statler, New York City, May 14-19, 1950. It is recommended that the Academy accept the invitation extended by this organization to exhibit.

Respectfully submitted,

MARGARET M. NICHOLSON, M.D., *Liaison Officer*

It was the action of the Executive Board that there be no exhibit by the Academy at the International and Fourth American Congress of Obstetrics and Gynecology to be held in the Hotel Statler, New York City, May 14-19, 1950, but that the matter be publicized to the members who might wish to exhibit individually.

National Society for Crippled Children and Adults

Subsequent to the last report, in which the purpose of the National Society for Crippled Children and Adults to establish a research program in services for the handicap was discussed, your Liaison Officer has forwarded 5 communications from various individuals or organizations who felt that their particular projects might receive aid and support from the National Society for Crippled Children and Adults.

I have conferred on 2 separate occasions with the publicity office of the Society concerning various news releases of pediatric interest.

Respectfully submitted,

GEORGE F. MUNNS, M.D., *Liaison Officer*

REPORT OF THE NOMINATING COMMITTEE

RECOMMENDATION:

For Vice-President (President-elect):

Dr. Paul W. Beaven
Rochester, N.Y.

Respectfully submitted,

A. WILMOT JACOBSEN, M.D., *Chairman*
WILLIAM P. BUFFUM, M.D.
JOSEPH STOKES, JR., M.D.
ROBERT C. HOOD, M.D.
BENJAMIN HOYER, M.D.
H. KENT TENNEY, JR., M.D.
PARK J. WHITE, M.D.
WILLIAM W. JONES, M.D.
LEOPOLDO L. BENEDETTI, M.D.

It was moved, seconded and carried that the report of the Nominating Committee be accepted. The Board recessed at 10:20 P.M. to reconvene on Sunday morning at 9:00 A.M.

Sunday, Nov. 13, 1949

The meeting was called to order by the President at 9:15 A.M. There were present, in addition to the Board and the Alternate District Chairman regularly attending. Drs. Frank Lancaster, Hugh McCulloch, Harold Dargeon, John Hubbard, John K. Glen and Joseph Wall.

REPORT OF THE EDITORIAL BOARD OF "PEDIATRICS"

The addition of 3 new members to the Editorial Board has increased the efficiency of the processing of manuscripts and has broadened the interests of the Board. Two changes have been made in the personnel of the special feature sections—Dr. Paul A. Harper has been appointed to succeed Dr. Edwards A. Park and Dr. Myron E. Wegman to succeed Dr. Leona Baumgartner. Both Dr. Park and Dr. Baumgartner have resigned. Dr. Harper has also succeeded Dr. Park as a member of the Editorial Board.

Conferences between the Editorial Board and the Publication Committee will continue to develop plans for publication of PEDIATRICS and for strengthening its financial position. Close cooperation exists between the 2 groups.

The presence of the Editor-in-Chief of PEDIATRICS on the Program Committee of the Academy has proved satisfactory from the standpoint of arranging the program for the meetings so that papers may be published in PEDIATRICS. Experience shows already that there will be better programs and that plans for publication will be better.

The Editorial Board continues to find unusual interest and support from many chairmen of the Academy committees and, in special instances, from individual members of the Academy. This auxiliary service has proved to be most helpful in editorial procedures and has brought to PEDIATRICS a great deal of expert advice and direction.

The format of PEDIATRICS has been changed with volume 4—the paper stock with a finish surface makes a better reproduction of illustrations, especially roentgenograms, and the additional cost is slight. The outside cover has been changed in several details with a more pleasing effect on the eye. Printed page of text will be changed in the future when costs permit.

Respectfully submitted,

HUGH MCCULLOCH, M.D., *Editor-in-Chief*
Editorial Board
C. ANDERSON ALDRICH, M.D.
ALLAN M. BUTLER, M.D.
HAROLD K. FABER, M.D.
ARILD E. HANSEN, M.D.
PAUL A. HARPER, M.D.
L. EMMETT HOLT, JR., M.D.
RUSTIN MCINTOSH, M.D.
IRVINE MCQUARRIE, M.D.
HERBERT C. MILLER, M.D.
RALPH PLATOU, M.D.
GROVER F. POWERS, M.D.
JOSEPH STOKES, JR., M.D.

It was moved, seconded and carried that the report of the Editorial Board be accepted and approved, with the appointment of Dr. Francis F. Schwentker of Baltimore to fill the place on the Board vacated by the death of Dr. C. Anderson Aldrich.

It was moved, seconded and carried that there be no future appointments to the Editorial Board without the submission of 3 names to the Executive Board.

REPORT OF THE COMMITTEE ON LEGISLATION

Many legislative bills, in which the members of the Academy may have interest, now before the Congress and its committees have been more or less dormant during the past few months.

It is doubtful that the Administration's compulsory health insurance bill, S. 1679, will have congressional consideration on the floor during the second session of the 81st Congress although extended hearings have been held during its first session, and a congressional group has returned from abroad where it surveyed the various systems of socialized medical care now operating in certain foreign countries.

Members of the Committee on Legislation have had the opportunity to study and report to its chairman upon S. 2352, introduced by Senator Pepper on July 29, 1949, a bill "To provide for research in child life and grants to States for maternal and child health and crippled children's services."

The first portion of this dual bill, Title I, includes in general the features of S. 904, approved by the Executive Board in Atlanta, acting for the Academy in the interim between annual meetings. This Title enlarges the functions of the Children's Bureau as outlined in the organic Act of 1912, relating to studies, surveys and reports on child health and expands the scope of such duties.

The second portion of this bill, Title II, would remove to this new bill parts 1 and 2 of Title V of the Social Security Act of 1935 (as amended) which are concerned with legislation and appropriations for maternal and child health and crippled children's services, together with increased appropriations for these various services.

Four members of the Committee on Legislation approve of the principles of this bill, one member dissenting. The chairman of the committee would ask that S. 2352 be presented to the Executive Board and the Academy at the San Francisco meeting, for the instruction of the committee.

The omnibus health bill, S. 1679, Title VI, from which Title II of S. 2352 has been lifted, contained a section under approval of State plans as follows: That determination as to the children to be furnished services under the plan . . ."without regard to economic status." This objectionable phraseology has been removed from the bill now under discussion.

S. 1411, the School Health Services bill, was passed by the House Committee on Interstate and Foreign Commerce, which held extensive hearings but has failed to report out the bill. At the hearings the chairman of the Legislative Committee strongly opposed 2 features of the bill as passed by the Senate, namely, Section 6, (a) (1) (C), which would extend to the States the privilege of giving FREE treatment to ALL children. Objection was also made to an amendment fathered by the Christian Scientists and included by the Senate which would exclude children of parents of that religious faith from the provisions of the bill. We offered to the House committee the following amendment: "In Sec. 6, page 6, line 21, after the word 'program,' insert 'Provided, further, that each State in its program should insist that such examinations as are necessary be made of all children to detect and exclude from school cases of communicable diseases.' "

S. 1453 and H. R. 5940, Aid to Medical Education, passed the Senate on Sept. 23. A committee of the AMA assisted the sponsors of S. 1453 in redrafting this bill after the hearings but the committee registered its opposition to the bill's final form because schools of osteopathy are included.

Respectfully submitted,

JOSEPH S. WALL, M.D., *Chairman*
PHILIP S. BARBA, M.D.
COURSEN B. CONKLIN, M.D.
HARVEY F. GARRISON, M.D.
PAUL HARPER, M.D.

It was moved, seconded and carried that the report of the Committee on Legislation be accepted.

The motion was made, seconded and carried that it be the function of the Committee on Legislation to analyze and comment on all bills pertaining to child health, and that such information be distributed to the membership in such manner as it deems wise.

REPORT OF THE COMMITTEE ON TUMOR REGISTRY

A conference of the Committee members in New York was held Sept. 26, 1949.

The following cases have been added to the Registry since the report of May 20, 1949:

Lymphosarcoma, jejunum	8 yr.
Rhabdomyosarcoma, embryonal	6 mo.
Rhabdomyosarcoma, embryonal	3 yr.
Neuroblastoma	4½ yr.
Hypertrophic hemangioma	11 mo.
Lymphangioma	3½ yr.
Teratoginous cystoma	9 days
Fibrous dysplasia	6½ yr.
Trichoepithelioma (Brooke tumor)	13 yr.
Medulloblastoma	8 mo.
Wilms' tumor	9 mo.
Wilms' tumor	7 yr.

Changes in Committee: Dr. E. Clarence Rice of the Children's Hospital in Washington, D.C., has been appointed a member of the Consulting Board of this Committee.

Proposed Registry of Juvenile Pathology (see chart): An accurate idea of the opinion of the membership of the society regarding the proposal cannot be obtained from this sampling. Some guides for present and perhaps subsequent action are suggested by the results.

VOTE ON PROPOSED REGISTRY OF JUVENILE PATHOLOGY

	Inquiries	Replies	Approve		Disapprove	Equivocal
Pediatric Department Heads	72	31	24		6	1
			Under Jurisdiction of American Reg. of Pathology	Other		
			19 (5 with reservations)	5		
Children's Tumor Registry Committee	17	16				
Academy Members (4)					2	2
Consultants Pathology (7)			6		1	
Other (5)			3			2
Totals	89	47	28	5	9	5

1. There were 31 replies (43%) from the pediatric educators to the 72 questionnaires sent out. Of these, 24 (77%) favored the establishment of a Registry of Juvenile Pathology. Nineteen of the 24, 5 with some reservations, favored the American Registry of Pathology as the organization to sponsor. Of the 12 consultants of this Committee (non-Academy members), 9 also favored the American Registry of Pathology.

Conclusion: Of the educators interested in the establishment of a Registry of Juvenile Pathology, the American Registry of Pathology is the organization favored by a majority.

2. Six pediatric educators, 2 Academy Committee members, 1 committee consultant, a total of 9, disapproved of the proposal. One pediatric educator, 2 committee members and 2 committee consultants voted equivocally.

Conclusion: There is not a unanimous opinion that the establishment of a Registry of Juvenile Pathology is necessary. Sufficient doubts are raised by the dissenters concerning the advisability of such a Registry to warrant the following recommendation:

Recommendation: The sponsorship of a Registry of Juvenile Pathology by the American Academy of Pediatrics is not recommended at this time. Action upon the proposal may be taken at a subsequent date, if the need for such sponsorship becomes evident.

Grant-in-Aid: An application to the Babe Ruth Foundation for a grant-in-aid for the work of this Committee has been approved.

Special Committee for the Study of Radiation Effects in Childhood: No meeting of this Committee has been held since March 3, 1949.

Respectfully submitted,

HAROLD W. DARGEON, M.D., *Chairman*
RALPH N. BARLOW, M.D.
F. ELMER JOHNSON, M.D.
GEORGE D. JOHNSON, M.D.
HAYES MARTIN, M.D.
FREDERICK H. WILKE, M.D.

Consultants

WILLIAM G. HEEKS, M.D.
JOHN M. KENNEY, M.D.
JAMES P. SIMONDS, M.D.
CHARLES A. WALTMAN, M.D.

It was moved, seconded and carried that the report of the Tumor Registry Committee be accepted.

It was moved, seconded and carried that the Academy approves the publication, by the Committee on Radiation Effects in Childhood of the Tumor Registry Committee, of their recommendations in this particular instance; namely, that no research study with radioactive isotopes shall be undertaken on pregnant women unless it cannot first be done on animals; secondly, the study is approved by the Committee for Human Use of Radioactive Isotopes of the Atomic Energy Commission.

It was decided to hold over until the June meeting the question of a new type of membership as suggested by Dr. Vernon W. Spickard.

It was moved, seconded and carried that the Academy would add its name to those of sponsors of the New England Speech Association in conducting their survey of the speech and hearing handicapped of New England.

It was moved, seconded and carried that the 1951 meeting of the Academy would be held in Toronto.

It was decided to send out a mimeographed proposed agenda to the entire membership one month before the meeting.

The meeting adjourned at 12:15 P.M. to reconvene at 9:15 A.M. Tuesday morning.

Tuesday, Nov. 15, 1949

The Executive Board reconvened at 9:45 A.M., the President presiding.

It was suggested by Dr. McCulloch that the next time the Editorial Board submits its budget, a special sum be allotted for the members of the Editorial Board of PEDIATRICS; $10 for each editor which will be used to reimburse each one for the cost of his subscription to PEDIATRICS.

A telegram informing the Executive Board of the death of Dr. Stanley Nichols was read. It was moved, seconded and carried that a telegram of sympathy be sent to the family, flowers be sent to the funeral and that Dr. Grulee write a letter of sympathy to the family.

It was moved, seconded and carried that a committee of 3 members of the Executive Board be appointed at this time by the President-Elect, subject to approval by the Executive Board, to review and to report to the Executive Board, a candidate or candidates to fill the proposed position of Executive Secretary.

It was moved, seconded and carried that the President appoint a committee from the Executive Board to consider annuities under the proposed reorganization plan and consult with Dr. Grulee or any other valuable sources.

It was moved, seconded and carried that upon the acceptance of the report of the Reorganization Committee by vote of the members at the Business Meeting, the Committee be dissolved.

The matter of the Playtex Park Research Institute for research in pediatrics was discussed but no action was taken.

It was moved, seconded and carried that the Academy would not refund the Seminar Registration fees to Dr. William Champion, Dr. Rieta C. Hough and Dr. Robert C. Hood.

It was moved, seconded and carried that we concur in the request from the AMA that a regular liaison be established between the AMA Council on Medical Education and Hospitals and the Academy Committee on Medical Education, and that we appoint the Chairman of the Committee on Medical Education to act as liaison officer and attend the meeting between these 2 groups as requested.

It was moved, seconded and carried that an invitation be extended to the Council on Medical Education and Hospitals of the AMA to appoint a liaison officer to meet with the American Academy of Pediatrics' Committee on Medical Education, and that our Committee Chairman be so notified.

It was moved, seconded and carried that the Committee on Tumor Registry be permitted to use some of the grant allocated to it from the Babe Ruth Foundation for purposes of research if the administrators of this fund so agree.

It was moved, seconded and carried that Dr. Grulee will get from Dr. Dargeon the proposed budget for the Babe Ruth Cancer Fund for the Tumor Registry and present it to the Budget Committee for approval.

It was moved, seconded and carried that a committee be appointed by the President-Elect to investigate the status of the Tumor Registry Committee.

There was no action taken on the letter from Mr. E. A. Waite *re* the Hoover Report, requesting

the Academy to send a resolution to Congress "urging the Congress to make effective the recommendation of the Hoover Commission by enacting appropriate legislation."

American Medical Association

At the meeting of the American Medical Association in Atlantic City, I was delighted to find that the sentiment of the members and officers of the AMA towards the Academy had improved considerably since the meeting in Chicago in 1948. At that time, as you no doubt will recall, there was pending before the House of Delegates several resolutions which, if passed, would have been very damaging to the Academy. It was my privilege to have been instrumental in stopping or modifying several of these resolutions, some before they were presented to the House of Delgates and some after they had been presented. Having been a member of the House of Delegates of the AMA for many years, and having many personal friends among them, I had an advantage in being able to approach them on matters concerning the interest of both the Academy and the AMA. In fact, at the Chicago meeting of the AMA, I found several prominent members of the Academy who were very antagonistic to some of the officers of the Academy as well as the more recent actions of the Executive Committee relative to endorsing the report of the ICH Committee, with which you are all now very familiar. At the meeting of the AMA in Atlantic City, there was noticeably quite a change in the attitude of some of the officers of the Association as well as some of its members who were formerly antagonistic to certain individuals working with the Academy and some of its officers. However, I regret to say that there is still some antagonism on the part of some of the members of the AMA toward the Academy. There are many reasons expressed for this which did not have their inception in the action of the Executive Board in endorsing the report of the ICH Committee.

At our last meeting in Atlantic City, our President asked me to discuss some impressions I had relative to some policies of the Editorial Board of PEDIATRICS. I called the Executive Board's attention to a few things that I felt should be corrected in order to help the sentiment against the Academy among not only the members of the AMA, but also the members of the Academy. You know there is a section in our journal, PEDIATRICS, that is devoted to papers under the editorial head of Drs. Edwards A. Park and Paul Harper, which gives space to articles that are critical of the AMA. I called the Board's attention to this practice by our Editors, the propriety of which I considered questionable then, but I notice that they continue to publish such articles. The latest one of these occurred in the June 1948 issue of PEDIATRICS. The Editors gave much space to the introduction of the author, Dr. W. Montague Cobb, a Negro physician, and also more space to his paper. This doctor is very critical of the AMA and in fact attacks its constitution and by-laws and its constitutional precedent in the manner in which it accepts members. Of course, it is stated under the heading of all such articles that "Statements appearing in this column do not necessarily reflect the opinion of the Editors nor are they to be interpreted as the official opinion of the Academy." Notwithstanding this fact, you can readily see that there is some incentive for the officers and members of the AMA and the Academy to believe that if the Academy was not sympathetic to such opinion, they would not allow them to be published in their official organ.

I heard a number of men in the AMA and the Academy express their feeling toward such antagonistic articles. You know some of the officials and members of the AMA as well as the Academy have the idea that the Academy is essentially a mouthpiece of the Children's Bureau and you also know that they consider the Children's Bureau as having been very antagonistic to the AMA and its concepts relative to socialized medicine. Therefore, when articles appear in our official organ directly or indirectly linking it with the Children's Bureau, it immediately alerts certain individuals to become more antagonistic to the Academy on this account. You will notice in the article by Dr. Cobb, that he is quite complimentary to the federal administrator, Oscar Ewing, who has just recently received a rather sound thrashing from the Congress in the defeat of the President's reorganization bill. This accomplishment can be credited to the master campaign by the AMA against him and his proposed socialistic plans.

I am sure the members of the Executive Committee are familiar with other criticisms that are coming from our own membership relative to the proposed new reorganization which, if not handled with extreme caution, will incur more internal dissention and antagonism on the part of not only these but other members of our organization.

I think it behooves all of us who hold any strategic official position with the Academy to be extremely careful about our activities and particularly about the liability of entanglement with certain

individuals who are leaning too strongly toward socialized medicine in this country, or with those who are too closely allied with the groups that are supporting legislation leading to the accomplishment of some form of socialized medicine. An outstanding example of the unrest among the membership of the Academy and particularly among some of the State Chairmen is cited in the letter to our President, Dr. Sisson, from the State Chairmen of Michigan, Indiana, Ohio and Kentucky. I have heard expressions which were somewhat similar to those expressed in that letter to Dr. Sisson from other members of the Academy since the general circulation of that particular letter.

I feel that the Academy should move very cautiously toward adopting any radical reorganization plans until the membership as a whole shall become thoroughly familiar with what is proposed and that they should have an opportunity to study and discuss thoroughly the proposals before they are finally acted upon. I can see in this a very great liability for more antagonism and more criticism from other members of not only our organization, but perhaps of the AMA as well. In a general way, I feel that the Academy could have very much less grief if they would not take the lead in attempting to influence pending national legislation prior to action by the AMA. Since the AMA is the parent organization and one in which endorsement or opposition to all pending legislation should occur, I feel that we should not assume leadership in endorsing certain types of legislation that has not already had the endorsement of the AMA. For the Academy to progress for the good of all concerned, I feel that we should all work together in harmony and certainly as much as possible with one accord on questions which would be construed as controversial. To this extent, and for reasons that are apparent, I think that all controversial questions should not be allowed to be discussed in our official organ, unless these questions have first been passed upon officially by the Academy.

The Southern Medical Association has had the second week in November as an established time of meeting for the past 40 years. As you probably know, the Southern has a membership of around 9,000. Naturally there are hundreds of pediatricians throughout the southern states who are vitally interested in the Academy as well as the Southern Medical Association. They participate in the pediatric program of that organization and are vitally interested in it. Since it so happens that I have been one of the executive officers of the Southern for 12 years, and am at present the Chairman of the Board of Trustees, it will be impossible for me to attend the meeting of the Academy, since for some reason the meeting of the Academy has been set on the identical dates of the meeting of the Southern.

On behalf of the southern pediatricians who are members of the Academy and would like to attend both meetings, I trust that the Academy will change its time of meeting in the future to either shortly before the meeting of the AMA or to about the first week in October, which would allow sufficient time between the two meetings to accommodate the pediatricians in attending both meetings.

As your Liaison Officer, I assure you that it has been a pleasure to have served the Academy in this capacity ever since the creation of this particular office, and regardless of what may come or go, I shall always be available to do what I can for the best interests of the American Academy of Pediatrics.

Respectfully submitted,

HARVEY F. GARRISON, M.D., *Liaison Officer*

It was moved, seconded and carried that this report be accepted.

It was moved, seconded and carried that the ICH office operate on a total budget of $25,600, exclusive of the Director's salary. It was the consensus of opinion that readjustments within the budget would be properly made by the Director.

It was moved, seconded and carried that the President-Elect appoint a committee from the Executive Board to make recommendations for an Executive Secretary. Dr. Shaw appointed Dr. Kennedy, Dr. Bost and Dr. Barba on this committee.

It was moved, seconded and carried that $1,000 be allotted to the expenses of the committee to nominate the Executive Secretary.

Dr. Sisson appointed Dr. Oliver L. Stringfield to investigate the activities and personnel of the Tumor Registry Committee.

It was moved, seconded and carried that the Academy be empowered to solicit funds for the purpose of public relations.

It was moved, seconded and carried that the present Committee on Pan-American Scholarships be

replaced by a committee which will handle all Latin American affairs which concern the Academy. The members will be Dr. Grulee, Chairman; Drs. Hurtado, Barboza, McCune, Smyth and Christopherson.

It was moved, seconded and carried that the deadline for criticism of the Interpretive Report of the ICH Committee would be Jan. 15, 1950.

The method of publication of the Simplified Treasurer's Report to the membership will be left to Dr. Grulee and Dr. Martmer.

The meeting adjourned at 12:10 o'clock.

Wednesday, Nov. 17, 1949

A meeting of the new Executive Board was held at 4:30 P.M., Dr. Edward B. Shaw, President, presiding. The following were present:

Drs. Philip S. Barba; Harry Bakwin; Crawford Bost; Arthur H. London, Jr.; Thomas J. McElhenney; Roger L. J. Kennedy; Oliver L. Stringfield; Edward A. Wishropp; Edward B. Shaw; Paul W. Beaven; Preston A. McLendon; Eugene T. McEnery; James C. Overall; Clifford G. Grulee; Edgar E. Martmer; Marshall C. Pease.

It was moved, seconded and carried that the Committee on Reorganization be disbanded after acceptance by mail vote of the entire membership. (It was necessary to reaffirm this by the new Executive Board.)

It was decided that the booklet "The Child Health Record from Infancy to Adulthood" would be turned over to the Committee on Cooperation with Non-Medical Groups, since the Committee on Contact Infections was being disbanded.

It was moved, seconded and carried that Dr. James G. Hughes, Chairman of the Committee on Cooperation with the American Legion, would name his own members of whom the Executive Board should approve in advance.

Dr. Shaw appointed the new committee members as follows:

COMMITTEE ON COOPERATION WITH AMERICAN LEGION

Honorary Chief Liaison Officer, Dr. Edward C. Mitchell
Chairman and Chief Liaison Officer, Dr. James G. Hughes
Associate Liaison Officer, Dr. Lawrence F. Richdorf
(Dr. James G. Hughes to name his own members)

COMMITTEE ON COOPERATION WITH NON-MEDICAL GROUPS

Chairman, Dr. Gerald M. Cline
Dr. Sherod M. Billington
Dr. John E. Brown, Jr.
Dr. Samuel Karelitz
Dr. W. Eugene Keiter
Dr. Margaret M. Nicholson

COMMITTEE ON SCHOOL HEALTH

Chairman, Dr. Thomas E. Shaffer
Dr. Jessie Bierman
Dr. Albert D. Kaiser
Dr. Robert Macdonald
Dr. Harold H. Mitchell

COMMITTEE ON FETUS AND NEWBORN

Chairman, Dr. Stewart H. Clifford
Dr. Katherine Bain
Dr. Joseph C. Jaudon
Dr. John C. Montgomery
Dr. Howard J. Morrison
Dr. Charles A. Weymuller

COMMITTEE ON HOSPITALS AND DISPENSARIES

Chairman, Dr. Peter G. Danis
Dr. John A. Anderson
Dr. Montgomery Blair, Jr.
Dr. Clifford G. Grulee, Jr.

COMMITTEE ON IMMUNIZATION AND THERAPEUTIC PROCEDURES FOR ACUTE INFECTIOUS DISEASES

Chairman, Dr. Archibald L. Hoyne
Dr. William L. Bradford
Dr. Alfred E. Fischer
Dr. Aims C. McGuinness
Dr. John J. Miller, Jr.

COMMITTEE FOR IMPROVEMENT OF CHILD HEALTH (Office expires December)

Executive Director, Dr. John P. Hubbard
Chairman, Dr. Warren R. Sisson (1952)
Dr. Lee Forrest Hill (1951)
Dr. Frank H. Lancaster (1951)
Dr. Ralph V. Platou (1951)
Dr. Albert D. Kaiser (1950)
Dr. Warren W. Quillian (1952)
Dr. Vernon W. Spickard (1952)
Dr. Hulda Thelander (1950)
Dr. George M. Wheatley (1950)

COMMITTEE ON LEGISLATION

Chairman, Dr. Joseph S. Wall
Dr. William F. Burdick
Dr. Coursen B. Conklin
Dr. Harvey F. Garrison
Dr. John K. Glen
Dr. John P. Hubbard

COMMITTEE ON MEDICAL EDUCATION

Chairman, Dr. John McK. Mitchell
Dr. John A. Anderson
Dr. Russell J. Blattner
Dr. Robert B. Lawson
Dr. Mitchell I. Rubin
Dr. H. N. Sanford

COMMITTEE ON MENTAL HEALTH
(SECTION ON MENTAL GROWTH AND DEVELOPMENT)

Chairman, Dr. Milton J. E. Senn (term expires 1951)
Dr. Katherine Bain (term expires 1950)
Dr. William Langford (term expires 1950)
Dr. Benjamin Spock (term expires 1951)
Dr. Sherman Little (term expires 1952)
Dr. George H. Schade (term expires 1952)

COMMITTEE ON PEDIATRIC AWARDS

Chairman, Dr. Donovan J. McCune (Dist. II)
Dr. Waldo E. Nelson (Dist. III)
Dr. Henry G. Poncher (Dist. VI)
Dr. Ralph V. Platou (Dist. VII)
Dr. Robert C. McGahee (Dist. IV)
Dr. R. Cannon Eley (Dist. I)
Dr. Harold K. Faber (Dist. VIII)
Dr. George M. Guest (Dist. V)

COMMITTEE ON SCIENTIFIC EXHIBITS

Chairman, Dr. Tom Mitchell

BUDGET COMMITTEE

Chairman, Dr. Edgar E. Martmer
Dr. Lee Forrest Hill
Dr. George F. Munns

COMMITTEE (SECTION) ON ALLERGY

Chairman, Dr. Bret Ratner
Dr. William P. Buffum
Dr. William C. Deamer
Dr. Jerome Glaser
Dr. Lewis Webb Hill
Dr. W. Ambrose McGee
Dr. James C. Overall

COMMITTEE (SECTION) ON SURGERY

Chairman, Dr. Herbert E. Coe (term expires 1951)
Dr. Oswald S. Wyatt (term expires 1951)
Dr. Jesus Lozoya Solís (term expires 1950)
Dr. Robert E. Gross (term expires 1950)
Dr. William E. Ladd (term expires 1949)
Dr. Henry Swan, Jr. (term expires 1949)

Drs. Ladd and Swan to be reappointed for another term of 3 years; to expire 1952.

COMMITTEE TO INVESTIGATE SELECTION OF AWARD WINNERS

Chairman, Dr. Thomas J. McElhenney
Dr. Harry Bakwin
Dr. Paul W. Beaven

COMMITTEE ON PUBLIC RELATIONS

Chairman, Dr. Philip S. Barba
Dr. Oliver L. Stringfield
Dr. Edward A. Wishropp

"PEDIATRICS"

Editor-in-Chief
Dr. Hugh McCulloch

Editorial Board
Dr. Francis F. Schwentker (1952)
Dr. Allan M. Butler (1951)
Dr. Harold K. Faber (1950)
Dr. Arild E. Hansen (1951)
Dr. Paul A. Harper (1951)
Dr. L. Emmett Holt, Jr. (1952)
Dr. Rustin McIntosh (1950)
Dr. Irvine McQuarrie (1950)
Dr. Herbert C. Miller (1952)
(Appointments expire at Annual Meeting)
Dr. Ralph Platou (1952)
Dr. Grover F. Powers (1950)
Dr. Joseph Stokes, Jr. (1951)

Corresponding Editors
Dr. Richard W. B. Ellis
Dr. Alan Moncrieff

Contributing Editors
Dr. John P. Hubbard
Dr. Myron E. Wegman

COMMITTEE ON CARE OF EUROPEAN CHILDREN

Chairman, Dr. Carl H. Smith
Dr. Robert A. Bier
Dr. Walter Levy
Dr. Douglas D. Martin
Dr. Philip M. Stimson
Dr. Carl H. Laws
Dr. Rustin McIntosh
Dr. Lendon Snedeker
Dr. Joseph Stokes, Jr.

COMMITTEE ON GEOGRAPHICAL DISTRIBUTION OF PEDIATRICIANS

Dr. Otto L. Goehle

COMMITTEE ON RHEUMATIC FEVER

Chairman, Dr. Hugh McCulloch
Dr. Leon DeVel
Dr. John P. Hubbard
Dr. George M. Wheatley
Dr. Saul J. Robinson

COMMITTEE ON U. S. FOOD AND DRUG ADMINISTRATION

Chairman, Dr. Waldo E. Nelson
Dr. R. Cannon Eley
Dr. Charles McKhann
Dr. Gladys J. Fashena
Dr. William A. Reilly

LIAISON COMMITTEE WITH AMERICAN MEDICAL ASSOCIATION

Chairman, Dr. Philip S. Barba
Dr. William Weston, Jr.
Dr. Woodruff L. Crawford
Dr. Harvey F. Garrison

COMMITTEE ON LATIN AMERICAN AFFAIRS

Chairman, Dr. Clifford G. Grulee
Dr. Einor H. Christopherson
Dr. Adamastor Barboza
Dr. Felix Hurtado
Dr. Donovan J. McCune
Dr. Francis Scott Smyth

PUBLICATION COMMITTEE

Chairman, Dr. Frank H. Lancaster
Dr. George F. Munns
Dr. Lewis Webb Hill

PROGRAM COMMITTEE

Chairman, Dr. Edgar E. Martmer
Dr. Carl C. Fischer
Dr. Clifford G. Grulee
Dr. Hugh McCulloch

TUMOR REGISTRY

Chairman, Dr. Harold W. Dargeon
Dr. Ralph N. Barlow
Dr. F. Elmer Johnson
Dr. Hayes Martin
Dr. Frederick H. Wilke
Dr. George D. Johnson

Consultants,

Dr. John M. Kenney
Dr. Charles A. Waltman
Dr. James P. Simonds
Dr. William G. Heeks

NOMINATING COMMITTEE

Chairman, Dr. Dennis H. Kelly (Dist. VI)
Dr. J. Harold Root (Dist. I)
Dr. B. B. Breese (Dist. II)
Dr. Walter B. Stewart (Dist. III)
Dr. Luther W. Holloway (Dist. IV)
Dr. Paul Wooley, Jr. (Dist. V)
Dr. Harvey F. Garrison, Jr. (Dist. VII)
Dr. Carl G. Ashley (Dist. VIII)
Dr. Arturo J. Aballi (Dist. IX)

Pediatrics

VOLUME 5 MARCH 1950 NUMBER 3

SPECIAL SECTIONS

THE PEDIATRICIAN AND THE PUBLIC

AN OPEN FORUM

PAUL A. HARPER, M.D., *Editor*

Statements appearing in this column do not necessarily reflect the opinion of the editor nor are they to be interpreted as the official opinion of the Academy.

COMMUNICATIONS FROM HARRY H. GORDON, M.D., ROBERT L. STEARNS, FRED A. HUMPHREY, M.D., WARD DARLEY, M.D., AND ALLAN M. BUTLER, M.D.

INTRODUCTION

By HARRY H. GORDON, M.D.

THE following articles by Robert L. Stearns, President of the University of Colorado, and Ward Darley, M.D., Dean of the University of Colorado Medical Center, describe the thinking which spurs members of the faculty of the University of Colorado Schools of Medicine and Nursing to participate daily in community activities. Dr. Fred A. Humphrey, President of the Colorado State Medical Society, health officer and general practitioner in Ft. Collins, Colo., long interested in problems of rural medical care, presents the views of a practicing physician on community responsibilities.

As indicated by Dr. Darley, every modern medical center contributes to the community by training of personnel, by research, by setting standards of medical care. Dr. Harper's invitation for these articles, however, stems from his knowledge of the conscious attempt being made by this school to discharge its obligations. From the moment one joins the faculty one becomes aware of responsibilities which are partly those of any medical school, partly those of any state university. The state university, said President Stearns at a convocation of medical students and faculty, is only incidentally interested in improving

Dr. Gordon is Professor of Pediatrics, University of Colorado, Denver, Colo.

the earning power of its students by providing good technical education; its primary aim is to educate for good citizenship and service to the community.

Interesting results stem from acceptance of this philosophy. A group of faculty members, thinking not only of their own departments or segments of their departments, but of the whole school and the whole community, are willing to reorganize drastically the curriculum. The values of a multi-disciplined approach to medicine, emphasized by Dr. Alfred Washburn and the staff of the Child Research Council, are generally accepted, and department heads yield teaching hours to interdepartmental needs with a minimum of resentment. With the example of Dr. Florence Sabin before us, we assume responsibilities to the State Health Department, the Denver Bureau of Health and Charities, the local county health units, to federal agencies such as the U.S. Public Health Service, the Children's Bureau, the Veteran's Administration, the Army, the Navy, the Atomic Energy Commission, to the residency training programs of private hospitals both in Denver and other Colorado communities, to the National Foundation for Infantile Paralysis, to local voluntary health and welfare agencies, to industry.

So numerous are these that working days become too short and voices are heard calling attention to the more traditional role of the university. Dr. David Hawkins, Associate Professor of Philosophy, says in a recent report to the University of Colorado Senate: "The university is the embodiment of a popular determination to serve the highest ends of political democracy, through the growth of technical knowledge and the enhancement of moral and esthetic perception. (Our activities) . . . involve constant research, constant criticism, and constant generosity toward new ideas and programs of action." These words can well serve as a guide for both the medical profession and the medical school. If we meet this challenge by daily achievement for the community, we will re-establish confidence in our profession more effectively than by self advertisement which tends to confuse shadow with substance.

THE RESPONSIBILITY OF A MEDICAL SCHOOL AND OF THE MEDICAL PROFESSION TO THE COMMUNITY

A. The Viewpoint of a Layman

By ROBERT L. STEARNS

MY approach to this subject is that of a layman who has been privileged for a number of years to have been associated with a university which has as one of its constituent colleges a School of Medicine. Because of a very evident lack of professional qualifications, I shall confine myself to the broader aspects of the responsibilities of a university in the community and illustrate my views by reference to the medical school and its responsibilities.

In the early days in this country, a university consisted primarily of a community of scholars old and young, somewhat disassociated from the world about them and patterning their lives after the mode of life in the institutions in Europe and England. With the growth of the nation and the westward migration of people, state universities came into prominence. They were the products of the felt need of the people in each state where they were located. Originally they proceeded on the basis of the older pattern and con-

sisted primarily of groups of scholars associated together in the classroom, laboratories and libraries. The curriculum was formal and of rather set pattern. As time went on, however, new obligations created their own solutions. New colleges were added to the university structure, professional schools sprang up in the midst of the academic atmosphere, and the university proceeded to meet those demands of the localities in which they lived. In more recent years, the removal of the faculty and students from the ivory tower is very evident. Both the process of instruction and the work in research agencies make evident the close association between the learning process and the service to humanity. The function of the university today is to touch the lives of practically every person in the community which sustains it. In some instances the approach is direct through the classroom and the lives of young people. In others it is through the extension division's forums, discussions and meetings sponsored by the university throughout the area. In still others, it is through the research facilities of the university in its various departments, whether in the field of public health, physical science or the creative arts.

This activity has been greatly accelerated since the war. The relationship between the institutions of higher learning and the people of the community is much closer than hitherto. For example, the University of Colorado is the center of the Municipal League of Colorado, whereby information is furnished to the various towns and cities concerning accounting methods, purchases of equipment, etc. The Bureau of Business Research is concerned with unique trade area studies furnishing information to the various chambers of commerce of localities throughout the mountain region. The Extension Division holds classroom sessions in the various cities throughout the state for older people and others denied the opportunity of attending the formal classes on the campuses. The Engineering Experiment Station works with industry and supplies the need of small industry not having its own research facilities. The Medical Center in conjunction with other appropriate departments of the University is engaged in the study of human diseases, physical and mental, and in conducting discussion groups for doctors and nurses of various phases of illness affecting the health and lives of the people in the community.

These illustrations could be multiplied many times, but they are sufficient to show the new outlook of an institution which derives its sustenance from the people and assumes, therefore, its obligation to return advantages to the community which sustains it.

Moreover, the faculties in our schools and colleges include men and women with knowledge of our natural resources and with abilities to aid industrial groups in their development. It is of importance that these resources be used not only for the benefit of the present generation, but that they also be conserved for the benefit of future generations. As our country becomes more populous and as the needs of the people increase, it becomes more and more apparent that the present generation is in a very real sense the trustee of posterity. The conservation of natural resources becomes then not only a matter of goodwill but of the application of the informed intelligence. This mountain region being among the last to be settled is also one of the last to feel the impact of population demands. The conservation of water, the intelligent use of grazing facilities, the elimination of waste in our natural resources are all problems which confront the present generation. Their impact upon the old order is bound to build a sense of confusion and occasionally of irritation. As time goes on, however, men of goodwill will be brought together, solving their problems by use of the scientific means which lie at the hand of the present generation. These means are the product of research and development, much of which has come about through the growth of our institutions of higher learning.

But the greatest resource which we possess is the health and well being of our people. The responsibility for the training of future generations of men and women skilled in the arts and sciences of medicine, nursing and the allied fields is one which can be met only by the cooperative endeavor of the professional groups possessing these essential skills. One has only to go back to the Oath of Aesculapius to observe that the responsibility for the training of the young in the art and practice of medicine devolves upon those already familiar with the intricacies of the art. Hence the medical school must depend upon the profession of medicine for the supply of its instructors. In the early days most of these instructors were drawn from the practicing profession. With the increasing demands on the profession these men and women are unable to give as much time as formerly, and hence full-time members of the faculty have had to be appointed not only in the preclinical but in the clinical years of study. They alone, however, are unable to meet the responsibility without continuing aid from the members of the practicing profession. Hence the medical field is unique among the colleges of a university because, in its very nature, it requires the close continual collaboration between the full-time teacher and the practitioner. Neither can do it alone, but together they should be able to provide the nation with an adequate supply of skilled persons.

I say "should be able," because the matter is not as simple as the foregoing statement would indicate. The cost of medical education in recent years has risen many fold. The growth of specialties has required extended periods of education. The amount of time available for a practicing physician to discharge his life's work is more and more restricted. The increase in the population and the growing awareness of the necessity for health care of families and communities has thrown a responsibility on the profession unequalled in our nation's history.

And yet at the time when it seems the burden is already too great, our communities have yet another tremendous responsibility they ask of the medical profession and the universities. They ask that we help in solving some of the great perplexing problems of better housing, better education, better conditions so that more of our youth may grow up to be physically, mentally and morally healthy.

They should turn to the medical profession and the medical schools for this aid. What other profession is as well supplied with men of high purpose and the basic understanding of how each person develops, physically, mentally and morally? The great problems of the day call for the sharing of the talents and abilities of all of us, and the doctors should be among the leaders.

We have seen in recent years a growing and alarming trend toward having a great central government take over the responsibility for many of these social welfare activities. Much of this has come about because of our unwillingness to solve our problems ourselves in our individual communities, states and regions. The mass of people the world over have determined that they are going to have steady progress toward the desirable goals of human betterment. They look not at the means but the end.

We must take the leadership in solving the problems the mass of people feel must be solved, or they will take the means out of our hands. We must show that we are working for the same ends and that our means to reach them are better. An effective university today is in the forefront of this struggle. It possesses highly qualified people on its staff who can and should be used to even greater advantage to the public than is now being done. But they are only one part of a team. The practicing profession of medicine is another part. Their cooperative endeavor is essential to the common good.

B. The Viewpoint of a Practicing Physician

By FRED A. HUMPHREY, M.D.

The best way to explain or understand the responsibility of the medical profession to a community is to project yourself, either by imagination or in reality, into such a community. By so doing you become an intrinsic part of that community and as such have delegated to you certain interests and responsibilities which you must accept for the common good.

It is immaterial whether the community of which you become a part is an isolated rural community or a small neighborhood group of a greater urban population. The problems are never the same in any two communities and, even if they were, it is questionable if similar solutions could be applied which would be satisfactory. It is just as important that each community and each problem be considered as a separate entity as it is that each sick person be treated as an individual. The human element enters into the association of a physician to his community as much as the physician-patient relationship affects the proper medical care of the American public.

The doctor I have visioned in the following remarks concerning the responsibility of the medical profession to the health of the community is best exemplified by the present concept of a general practitioner. However, that does not mean that the requirements cannot be emulated by a pediatrician or a representative of any other special group in his contacts with a more limited segment of society.

To properly play the part of the general practitioner, a doctor must have the knowledge and inherent interests of at least three separate and distinct persons: (1) a physician, who has the responsibility of caring for the sick; (2) a health official, who advises the community on all matters relating to general health; (3) a citizen, who takes his rightful place as a leader in all questions of civic improvement.

Without fear of contradiction, I would consider his first duty to be that for which he has spent many years of his life in preparation; namely, the diagnosis and treatment of disease. He not only must have been thoroughly trained in the essentials of physical diagnosis and therapeutics but he also must show a continuing interest in the welfare of his patients by constant study of the more modern advances of scientific medicine. This is best accomplished by regular attendance at medical meetings and postgraduate courses.

If you were asked to define the practice of medicine, I am sure the great majority of you would define it as "The art and/or science of treating disease." In that definition, art holds equal prominence with science. In the old days of the horse and buggy, family physician type of practice, the art of medicine was probably of equal or greater importance than the science in the actual treatment of disease. During the past few years great strides have been made in the scientific fields of medicine with the discovery of many new "wonder" drugs and new methods of treatment. The art of medicine has not kept pace and some doctors now believe that it has been entirely lost and is no longer essential. In spite of the recent advances in chemotherapy and the trend toward more specialized care, the modern counterpart of the old family doctor is still the basic foundation of good medical care. No matter how efficient the scientific treatment may be, it is rendered more effective by the proper patient-physician relationship which allows the physician to make full use of his personality in obtaining and maintaining the maximum confidence and comfort of his patient.

The trend in medical education during the past two decades has developed according to a definite pattern. This modernization of teaching methods has resulted in a type of medical practice which emphasizes specialization and discourages general practice. Striving toward more perfection in teaching medical students, the natural inclination is to use doctors best qualified in the various fields or specialties as the instructors and lecturers. The inevitable sequence of this type of training is to graduate medical students who have the natural desire to emulate their teachers and become specialists in one or the other of the various fields. The desirability of maintaining this high standard of teaching is obvious and above criticism, as the medical profession wishes the undergraduate to receive the very highest type of education. Any improvement in the curriculum therefore cannot be made by a curtailment in the teaching by specialists. It should be accomplished by the addition to the staffs of our medical schools and teaching hospitals general practitioners who will lecture on the art as well as the science of medical care. It would become their duty and privilege to correlate the teaching of all the specialties, thereby causing the student to regard his patient in the light of total medical care.

In the past few years a few medical schools have instituted such a section on general practice, which, along with establishing a residency in general practice on an equal basis with residencies in other fields, has accomplished a great deal to balance the overemphasis on the desirability of specialization.

There is no doubt but the future teaching of medicine, of necessity, will become more and more scientific and specialized but the value of the patient-physician relationship should never be discounted or lessened in the present or future methods developed for the care of a sick population.

So much for medical education and the responsibility of the medical schools to the community. That part of this title will be covered in detail by Dr. Ward Darley who has had a wide experience in that phase of medical education. Let us pick up the medical student after he has completed his training and is ready to locate in the community in which he has chosen to live.

One of the most important decisions he will be required to make concerns the type of practice he wishes to develop whereby he can best fulfill his obligation to his community and to his family. During the past few years, group practice has been extolled as the panacea for all medical care ills of small communities both urban and rural regardless of size, shape or distance from other communities. This may be the proper approach in many larger communities but throughout the United States there are many small towns needing and deserving medical care that cannot adequately support more than one doctor. I would therefore like to present a plan of medical care which will adjust itself either to a town large enough to support any suitable number of doctors or a group of adjoining towns so small that they cannot maintain more than one or two doctors. It is conceded that a doctor in a small town must do general practice. No doctor has either the mental or physical stamina to keep thoroughly abreast of all the advances in the many special branches of medicine. In order to bring to each community the best possible medical care it is therefore necessary to copy the idea of group practice by doctors of various specialties without the actual formation of such a group. The answer is that each doctor, whether practicing in a large community or in adjoining small towns, does general practice with a particular leaning toward one or the other of the specialties. The majority of his postgraduate work would be done in the specialty he has chosen

until he has perfected himself to such an extent that the other doctors in his neighborhood will have confidence in his ability. He can then act as consultant for them in any difficult cases which require the services of a specialist and in turn call into consultation the other doctors in his vicinity who have chosen to do their postgraduate work in some other specialty. By such a system of cooperation among the doctors, the medical profession can discharge its obligation of furnishing the best possible standard of medical care to the community at the least possible cost to the patient.

The second responsibility is that of a health officer or a person interested in preventive medicine as contrasted to curative medicine. All too many doctors believe that their obligation begins only at the advent of illness. They are too busy caring for a sick child or adult to be bothered with the supposedly minor details which have to do with the prevention of disease. However, if a doctor is to accept the full responsibility to his community he not only must have a thorough knowledge of but also must take an active interest in all health activities which even remotely might have a bearing on the welfare of the people he has chosen to serve. It does not follow that the actual duties of a health officer should be assumed by every physician but, as the individual who has the most comprehensive knowledge concerning health matters, he should use that knowledge to the greatest benefit of the most people of his community. He should show a continuing interest and leadership in all problems which might affect community health by offering his service and professional advice to all voluntary organizations or legal bodies which show an interest in the health of the community. The various lay groups which deal with the control and eradication of such diseases as tuberculosis, cancer and poliomyelitis not only merit the support of the public in general but also deserve the constant guidance of the medical profession. If organized medicine is not willing to provide such guidance, then it should not object if one or more of these lay organizations establish a program with which it does not agree. Each of these groups not only desires but also deserves medical participation. See that our profession is represented at every health meeting even if you have to be that representative.

The third responsibility is that of a citizen. While it always should have been an obligation of major import, only during the past few years has it been brought to the forefront. The medical care and the health of the people have been the constant responsibility of the physician. Now he must fight to retain that responsibility in order to prevent its being usurped by governmental bureaus. In order to prevent such a socialization of medical care, practically all departments of organized medicine have instigated and developed educational and public relations programs. Such activities in the national and state societies should be vigorously supported and promoted by all members of the medical profession. However, the encouragement of such programs, either by passive or active participation, does not fulfill the responsibility of the physician if he is to take his rightful place as a citizen in his community.

The time has come when every doctor must stand up and be counted. For many years the men who sacrificed their time to carry on the business affairs of your society were called "Medical Politicians." Such persons were present in all societies, the American Medical Association and its component state and county societies as well as the organizations representing the various specialty groups. This name of "Medical Politician" was

meant as a stigma but now the doctors of America should be thankful that a few of their numbers had the foresight to offer their services for the good of all. By their actions they kept American medicine alive as definite organizations. We now should go one step further in action as well as in name calling and delete the word "medical" from the phrase. Then each and every doctor in the United States should join with the leaders and become a "politician."

Whether you like it or not, you are in politics and the sooner you realize it and act accordingly the better it will be for the health and welfare of your patients and neighbors. As a citizen you should take part in all activities of the community and not limit yourself only to the ones which have a direct bearing on health matters. Too few doctors are willing to serve as mayor of their town or on the town council. Do you know of a physician who is a member of a state legislature? Does a doctor represent your district in Congress? While members of the medical profession cannot and should not fill all these positions, there is no valid reason why they should not take an active part in selecting the person who is to represent them in the legislative halls of the town, county, state and nation in which they live.

This country achieved its greatness on the principle of free enterprise and can maintain its supremacy only by retaining the foundation on which it was built. The Bureaucrats of Washington have issued a challenge to the medical profession and as a result the doctors of America have been put on the firing line. They must carry their full responsibility as citizens or medical care as well as many other independent businesses will no longer remain free from total government control.

In lieu of a summary I will repeat an editorial printed last summer in *Industrial Medicine*. It aptly describes a duty which should be an obligation of each individual member of a medical society. It is based on that old familiar cry heard at every medical meeting, "Is there a doctor in the house?" I quote the editorial:

"In order that the physicians of the United States may preserve the standards of their profession and avert lay inspired chaos that threatens

In every lay assembly to talk about state medicine or its related panaceas, systems, or plans

At every legislative committee meeting to consider proposed bills—

In every council where the subject is part of the order of business and—

At all sessions of law-makers, from those of the Congress at Washington to those of the county boards and municipal councils at home—

Let there be a doctor in the house.

If he isn't invited, let him go anyway—crash the gate if necessary because he has the right to be heard. He *can* get in if he *wants* to get in. He ought to want to get in, *because he is the duly qualified representative of the public in medical matters.* Needless to say much more qualified and much more representative than the laymen who are leading the present agitation."

In conclusion let me suggest that the medical profession renew its pledge to the American people, that we will always adequately fulfill our responsibility of furnishing the highest standard of medical care possible to the various communities as long as we remain free and are not fettered by government regulations.

C. The Viewpoint of a Dean of a Medical School

By WARD DARLEY, M.D.

As soon as I began consideration of this subject I was impressed with the fact that while all our communities have certain common interests, resources, problems and ways of doing things, their modification by local variance is usually such that comparison is not practical. This is particularly true in the field of health service and medical care. While all communities may be similarly striving for high standards, they are very dissimilar in the way in which they put varying resources together in order to indulge varying interests and to meet varying problems. This is in line with typical American philosophy—high standards without standardization.

While the number of variables important to the resultant health service and medical care of any community are numerous, there are two factors that are obviously pertinent to this discussion: a medical school and the practicing physicians. Some communities have medical schools and some do not. While all medical schools are striving to do the best job possible in the training of personnel, no two are entirely comparable as to their resources and the manner in which they function. All communities have practicing physicians and, while it is safe to state that with the rare exception all are striving to render the best service possible, no two communities are similar in physician-population ratio or distribution or in the collective talents, interests and abilities of the physician group.

As a general thesis, I wish to submit that a primary responsibility of a medical school and of the practicing profession is to join with the community in the evaluation of resources and problems so that the best possible planning for health service and medical care will result. While this may not be a new concept, I know of very few communities where this is being done deliberately. Before such planning can be very effective, the powers-that-be in the medical school and the medical profession must come together, recognize and analyze the obstacles and collaborate in the development of acceptable philosophies and aims. This very procedure is just beginning in Colorado. It is too soon to report on any details of the considerations. It can be fairly stated, however, that definite obstacles do exist and that these must be understood and surmounted before common ground can be cleared for action. Obstacles that are basic must be sorted out from those that are secondary or symptomatic. Varying vantage points and the resultant philosophies and attitudes must be fully appreciated. Then and only then can a start be made in the direction of an adjustment toward philosophies and aims that can be shared in common.

In the meantime, while these discussions are under way, life has been going on for some time and must continue to go on. For many years both the medical school and the medical profession have existed side by side without any formal association and without recognizing that they have too much in common. This does not mean that numerous individual practicing physicians have not given generously of their time and energy to the work of the University of Colorado Medical School and its hospitals, clinics and other service programs; and it does not mean that both the medical school and the medical profession have not made commendable progress in discharging community responsibility.

Further discussion of the activities and responsibilities of the medical profession was

left to Dr. Fred Humphrey; the balance of this communication will concern itself with the current aims and activities of the medical school which I think are of importance to the welfare of our community. As this is done it will be noted that on occasion the school and the profession have joined in certain projects. These developments are recent and their apparent success encourages us to give consideration to a broader base of understanding and cooperation.

It should be obvious that the primary purpose of any medical school to any community is to train individuals to render health service and medical care. The implications of this statement are many because many categories of personnel need to be trained, because the training program must develop individuals capable of rendering efficient service in an ever changing scientific, social, economic and political world, and finally because of the complicated backdrop of teaching, research and service resources essential to an effective training program.

Physicians constitute but a small portion of the group involved in providing health service and medical care. While a medical school's primary concern may be the training of this group, its facilities must be available for the education of other personnel such as nurses, social workers, technicians, administrators. This is as it should be, for the health service and medical care team must eventually work together in a service situation. Why should not the categories concerned learn to work together during their preservice training? In the present discussion, this extended responsibility of a medical school will not be discussed in detail; it will be apparent, however, that a great deal of what I have to say about the training of physicians will be applicable to the training of all categories of personnel.

In the training of physicians the community responsibility of the medical school begins with the original selection of the student who is to study medicine. While an educational experience may be directed to stimulate and develop such qualities as intellectual honesty, a high moral code, proper motivation, social consciousness and other desirable personality traits essential to the true physician, the capacities necessary for these attributes are dependent upon developmental factors over which no medical school has any direct influence. Consequently, the admissions machinery of the school must select students in whom these capacities are already present. In the dim light of our present-day knowledge about selection methods, this is a difficult assignment.

Given the student with the proper potential for medicine, the four years of medical school are the most crucial in the training of a doctor, and herein lies the school's greatest community responsibility. This over-all responsibility of the school is to produce a professional individual capable of functioning in an intimate relationship with human beings and the communities in which they live in a manner that justifies the greatest of trust and confidence. This implies an educational experience that presents a basic minimum of factual information, carefully selected from a veritable mass of possibilities, and this presented in such a way as to stimulate and broaden, not limit, the individual's range of interest, and in such a way as to instil a perpetual desire to learn. At the University of Colorado an attempt is being made to present medicine as a wide, unisolated segment of human biology. With this approach the student's interest in human growth, adaptation and development from the structural, physiologic and psychologic standpoints is readily challenged. The importance of the interplay between the human organism and its environment as a basis for understanding health and disease is readily appreciated when

the student realizes that disease is but one of the many reactions that can take place in the human organism in response to environmental stimulation—whether the stimulation be internal or external; whether the reaction be anatomic, physiologic or psychologic. With this as a background, the student then is ready to move into a consideration of the wide field of clinical medicine without isolating his thinking and interests from other important tangential aspects of human biology. In other words, he will realize that there are such things as social and community health and sickness and that these problems have as much claim on his interests and abilities as do those of the individuals for whom he is responsible.

In our effort to accomplish all this we are attempting to develop every undergraduate medical student as if he or she were to enter general or family practice. This means that the consideration of specialty technics and procedures are properly minimized. We consider it our responsibility to provide a broad base that should be common to all physicians, regardless of what their ultimate sphere of formal professional activity may be. This type of training, with a proper balance between the presentation of factual material on the one hand, and stimulation and inspiration in the place of "spoon feeding" on the other, is far from easy. Without going into details of the modus operandi for maintaining this balance, and so as to keep somewhat within the confines of my subject, I wish to submit that perhaps the most powerful teaching force at our disposal is that of precept and example. This applies to the practicing profession and the ancillary groups rendering other aspects of health service and medical care just as much as it does to the medical school and its faculty. I do not think that any other community responsibility for any of these groups can transcend this in importance. In other words, both the doers and the teachers (and whether they are aware of it or not, both practitioners and faculty are active in both areas) are obligated to conduct themselves, individually as well as collectively, to the end that the service situation in which they find themselves can be used, if only by example, for teaching purposes.

These statements ordinarily would lead into a detailed discussion of the milieu of an adequate educational program, but first it is necessary to finish the outline of a medical school's responsibility in the training of the physician group. I refer to intern, graduate and postgraduate education. In passing, however, I submit that the educational philosophy mentioned above in relationship to undergraduate medical education also applies to these activities, perhaps even more so.

From the educational standpoint, the internship is currently presenting difficult problems. There are many more internships available than there are interns. As a consequence, many of our private hospitals are not able to obtain enough interns and the few interns obtained must work so hard that the experience is completely robbed of educational value. From the hospital's standpoint, it should be obvious that this situation represents a handicap to good service. It seems to me that given a community with a medical school, the proper cooperation between the school and the medical profession should make it possible to remedy such situations and thus jointly to render real community service. During the past year the University of Colorado has made real progress in this direction, and as a result of a pooling of the educational potential of the school and the staffs of the private hospitals, the private hospitals have obtained their full quota of interns for the first time in many years. The survival of this arrangement will depend upon the provision of a real educational experience for the interns involved.

Since the end of the war graduate training in medicine has been developing rapidly as a field of major responsibility for both the medical schools and the privately controlled hospitals. The time has come when several years training beyond the intern year is almost a "must" for every medical graduate. Thus it should behoove every institution interested in graduate training to develop both educational and service programs of the highest caliber. Here again, the pooling of medical school and hospital staff resources should potentiate both of these ends. The implications of such an activity in terms of community welfare speak for themselves. Here again, during the past year Colorado has made progress and the results to date have been more than gratifying. In fact, the point has been reached where the demands upon the program are far exceeding our ability to keep up.

While I am discussing this question of graduate education, I feel that the adequate training of men and women for general practice deserves emphasis. During the past few years specialty training and practice have developed rapidly, so that the point is being reached where the family physician, the one who should shoulder the burden for the direction of the broad aspects of health and medical care, will disappear from the scene. I feel that the only way to counteract this trend is to put proper emphasis upon the need for such physicians, and at the same time to emphasize the importance of providing special training for this special assignment. Specifically, this assignment should involve the development of abilities that make it possible to provide positive health counseling from birth to death and also proficiency in the diagnostic and therapeutic aspects of pediatrics, internal medicine, geriatrics and psychiatry, and all of this superimposed upon interests and knowledge that will make it possible to bring all available community resources to bear upon any individual or family health problem. Also, this group of physicians is the logical one to provide leadership in the direction of correcting, modifying or developing community factors and resources that in themselves are important to better community health.

A three year general practice residency has been in effect in Colorado for the past three years, development of which is rapidly involving more and more community interest and cooperation. Every individual that has completed this residency has settled in Colorado or some other Rocky Mountain community where his or her services are desperately needed. We feel, therefore, that in developing this program a very important community responsibility is being discharged.

Rapid developments in the scientific aspects of health and medical care are such that the question of continuing education for men and women in active practice is fast becoming one of first importance. While the organization and presentation of short, formal postgraduate courses is of importance (over 1,000 doctors have attended these courses during the past 2½ years), this activity is not to be compared in value with postgraduate stimulation that can be carried to the hospitals and communities of the practicing physicians themselves. Programs embodying this type of educational activity are developing rapidly over the country and, in keeping with this trend, the Colorado medical school and profession are working together in an interesting local program. Time and space will not permit a further elaboration of this work. Its importance as part of an over-all effort to meet the challenge of community responsibility should be self evident.

I come now to a most pertinent part of my assignment: a discussion of the importance

of the proper backdrop, other than the points that have been made already, for the type of educational responsibility I have attempted to outline.

Research is an essential part of this backdrop. Recent advances in scientific medicine have largely resulted from research that has been done in our universities and their medical schools. This represents an assignment of community responsibility that has been well done. Most of this research has been of a laboratory and clinical type, the general nature of which is fairly well understood. Future scientific progress will obviously depend upon the continuation of this type of activity and, while this may be taken as an important segment of a medical school's responsibility to the community and the medical profession, the community (including the medical profession) must play its part in according these activities their due support.

In addition to the usual types of laboratory and clinical investigation, another type of research is beginning to loom up in importance—the survey and statistical type of research aimed at studying socio-economic factors in the control and management of health and disease, and also in the administrative and professional activities related thereto. The successful execution of this type of research will depend upon the cooperation of all elements in our society but the responsibility for leadership essentially rests with the medical profession and the medical schools. Many communities can now cite examples of this type of research. Denver has just completed a morbidity survey on multiple sclerosis, and a survey of heart disease in children throughout the State of Colorado is just getting under way.

While research per se is of importance to the continued progress of scientific medicine and represents a responsibility to the community of the first magnitude, it must not be forgotten that the conduct of research is essential to the vitality of a medical school faculty, particularly if said faculty is to keep abreast with scientific progress and is to maintain the alert and questing attitude essential to effective teaching. Finally, research in itself represents an invaluable teaching medium, particularly for those graduate students at the basic and clinical science levels.

While a certain amount of formal classroom and laboratory-teaching and the stimulating research atmosphere is essential to any educational effort in the field of health service and medical care, this effort will result in very little that is effective unless it can be crystallized within a properly supervised service situation that involves a maximum of student participation and responsibility. The term "service situation" must be used in a very broad sense and should include, in addition to work in the clinics and hospital wards, an opportunity to see and take part in activities that involve community resources and that bring such resources to bear upon the solution or modification of individual, family and community problems in the field of health and preventive service, as well as in the field of disease control and management. In other words, if environmental medicine is to be taught, the environment must be used as a teaching laboratory.

For the past few years the Regents of the University of Colorado have recognized that many resources for community welfare exist in the University, and have encouraged the extension of these resources beyond the confines of the campus into the community, and this in such a way as to potentiate, not compete with, existing community activities. The resources of the School of Medicine and its hospitals lend themselves particularly well to this goal, and as a result, there are now more than 60 projects, involving the annual expenditure of several hundred thousand dollars, each of which involves one or

more units of the University Medical Center and one or more community agencies. All these activities benefit immeasurably from the medical school affiliation and, needless to say, each activity immeasurably increases the teaching, research and service potential of the Medical Center.

This last statement leads me to the conclusion of this communication. It may sound trite to state that in unity there is strength, but in dealing with problems of individual and community health and sickness, the pooling of resources, with their reasonable coordination, should be considered as a responsibility of every individual group or agency that possesses such resources. If health services and medical care were not effective, this statement would not be justified; but since they are effective, it follows that health and sickness are the reasonable concern of every individual. The possession of any resources or ability implies responsibility. Schools of medicine, the medical profession and its ancillary groups, and our communities at large all possess resources that can augment any system of health and medical care. Our composite society, the medical profession and its entourage and the educational system basic to health and medical service could not exist as we know them without the support which each gives to the other. In other words, while this assignment was limited to a consideration of the responsibility of a medical school and the medical profession to the community, I do not want to close without injecting the reminder that the reverse is definitely implied: the community must assume definite responsibility to its medical school and its medical profession. As far as medical education is concerned, I wonder if our nation-wide communities are as aware of their responsibilities as they should be. I believe that this question is justified because over the years the financial support of most of our schools of medicine, from the relative standpoint, has not kept pace with the responsibilities which they have been assuming, and I believe that if the medical schools of our nation are to discharge the responsibilities of which they are capable, the challenge of their support is one that should receive the serious consideration of every community.

DEAR DR. HARPER:

There is an error in the next to last sentence of my letter to you published in the December 1949 issue of PEDIATRICS (vol. 4, p. 845), to which I would like to call attention. The sentence as printed contains the following phrase, "altogether unjustified fear." It should have read, "altogether not unjustified fear." The change in meaning, at least to me, matters considerably, for I think doctors should be concerned about being underpaid under insurance or prepayment medical plans. Inadequate remuneration would almost certainly mean deterioration of service. The low remuneration of public school teachers and government employees in general justifies some fear that it may happen in medicine. We doctors must do what we can to see that this does not happen. As indicated in my letter, the fee-for-service remuneration of doctors under prepayment plans would almost certainly result in underpayment.

(signed) ALLAN M. BUTLER, M.D.
Boston

TRENDS

By JOHN P. HUBBARD, M.D., *Contributing Editor*

This and subsequent descriptions of events and trends are intended to be unbiased and factual, presenting both sides of controversial matters so that conclusions may be formed from critical appraisal of things as they are. These statements do not necessarily reflect the opinion of the writer nor are they to be interpreted as official opinion of the Academy.

REGIONAL PLANNING IN DISTRICT III

ATTENTION has frequently been called to the two most prominent needs revealed by the Academy's Study. The first calls for a better distribution of pediatric services; the second calls for more attention in undergraduate and graduate training to the health supervision of normal children and the practical aspects of pediatric practice. To meet this two-fold need, the Academy has emphasized the importance of regional planning, or decentralization, if this latter term is preferred. In order to serve as a testing ground, a program has been instituted in Pennsylvania, New Jersey and Delaware, District III of the Academy. One aspect of this program has been provision for a resident to spend a three month period serving two community hospitals which are located reasonably close together. The Montgomery Hospital at Norristown and the Phoenixville Hospital in the town of the same name were selected for this purpose. These two hospitals are both about 25 miles from Philadelphia and about eight miles from each other. A pediatric resident, Dr. Ronald M. Bernardin, who had already completed his residency training for Board Certification, was given the first appointment in this part of the program. The following two letters, one from Norristown and the other from Phoenixville, are an indication of the program's value from the point of view of two communities:

DEAR DR. HUBBARD:

On behalf of the pediatric staff and the general staff at the Montgomery Hospital, I wish to express my appreciation of the District III program for supplying us a pediatric resident during these last three months. The resident, Dr. Bernardin, whose services we have shared with the Phoenixville Hospital, had been well trained in all branches of pediatrics. He was well liked and accepted by all the men of the entire staff in our hospital and I have been told the same holds true for the Phoenixville Hospital. Everyone is enthusiastic about continuing this type of service.

The amount of time spent in each hospital varied depending on which had the cases requiring the most attention. However, since Montgomery Hospital is the larger of the two, more time was probably spent there.

The two hospitals agreed as to the financial responsibilities, a salary plus some travelling expenses being paid by both hospitals.

Both hospitals are approximately a 45 minute drive from the center of Philadelphia, but the parents of our patients prefer to have their children as near to home as possible when they are ill so they can more readily be visited. Many of these patients required intravenous therapy or other technical procedures which could not be done by the usual general hospital intern.

In the past, since it is impossible for the chief of service to handle both a busy practice and the duties of a resident, these patients who require special care were usually sent immediately to the larger teaching hospitals in Philadelphia. Now that we have the services of a resident, these cases were kept in our hospital with gratifying results.

Many of these cases were presented by the resident and discussed at regular pediatric conferences attended by the interns, nurses and visiting men. The interns were particularly grateful to Dr. Bernardin for his instruction. Usually the visiting chief has a limited time to spend making rounds so that not as much time could be given to instructing the interns as was desired.

The general practitioner also benefited by having this trained resident care for his private pediatric cases in the hospital.

The consulting staff as well as the laboratory and x-ray departments in both of these hospitals are excellent so that the majority of cases can be studied satisfactorily. Of course, there are some unusual studies that can only be done in the teaching institutions. Our equipment, particularly in the Montgomery Hospital, is better than in many of the large city hospitals and I am told we have better nursing care with more nurses available than in many of the city hospitals.

At Montgomery Hospital there are 20 pediatric beds and 40 bassinets. At Phoenixville there are 8 pediatric beds and 25 bassinets.

This year we had a late polio epidemic with an equal number of adult and child cases admitted to our isolation section. Since Dr. Bernardin had been well trained in the care of these cases while at the Municipal Hospital, he was put in charge of all cases. Everyone was well pleased with the successful coordination that resulted.

All newborn infants were examined by the resident regardless if private or ward patients. We all know this should be routine but in our hospital, as in many others where interns are now limited in number and most of the babies are delivered by general practitioners, many of the babies are never examined during their stay in the hospital.

Thus far it sounds as if only the hospital has benefited from the resident's presence. But I believe that he learned a great deal while working with us. His eyes were opened by the great variety of cases on our service. He had to accept more responsibility and had a closer contact with the parents. I think he realizes how important it is to have adequately trained pediatricians in the smaller towns where people are now becoming more specialist minded. Most parents don't want to take their children into the city to see their pediatrician and when they are ill they want the same physician caring for them in their local hospital. Many times this can be done without the aid of a resident but we all realize how much easier and better it can be done when there is a trained resident on hand to carry out the necessary technical procedures.

Unfortunately at present no credit toward certification by the specialty board has been given to this man for his excellent work. But I know he has seen just as many interesting and unusual cases and has learned just as much in his three months with us as he would have learned in any of the teaching institutions in the United States.

I do not believe any resident should spend a whole year in one small hospital. A period of three months would be quite adequate and would stimulate him in his work on returning to the larger institution.

Many of the hospitals near the large cities are unable to care for many pediatric cases even though good pediatricians are on service, because of the inability of the general

intern to carry out common pediatric technical procedures. As a result these cases are sent into the teaching institutions, causing over-crowding.

I believe a system with a resident servicing at least two and possibly three small hospitals in short distances of each other would improve the general pediatric care of patients, keep the visiting men informed as to the latest developments in the larger institutions and prepare the resident for going out into practice for himself.

I would like to see the resident receive credit toward his board certification and, if at all possible, the continuation of this type of service in our hospital. Everyone feels it has been a great success.

(signed) THOMAS T. KOCHENDERFER, M.D.
Norristown, Pa.

DEAR DR. BROOKS:

With the departure of Dr. Bernardin last week, we finished the first three months' trial of the shared pediatric residency. I thought you might be interested in some of the impressions the program has made.

We had the first pediatric conference which has been held here in some years. At its close the hospital staff requested that at least one of our monthly staff meetings hereafter be devoted to pediatrics.

We have revised the routines and procedures in the newborn nursery. Dr. Bernardin attended our Nursery Committee meetings and offered a number of excellent suggestions.

In the daily hospital care of our pediatric patients, the resident carried out all treatments; did history and physical examinations; took charge of all house cases, both newborn and pediatric ward; and gave to the staff members the benefits of his more recent training.

I, personally, have greatly appreciated Dr. Bernardin's help at Well-Baby Clinic. We have each spent two hours a week as compared to the one hour weekly previously and have almost doubled the number of infants and preschool children attending.

There has been an up-surge of interest in pediatrics. The medical staff is heartily in favor of continuing the program and was delighted to hear that Dr. Eister would be with us for the next few months.

My personal thanks to you for making all this possible.

(signed) LOLA S. REED, M.D.
Phoenixville, Pa.

PUBLIC HEALTH, NURSING AND MEDICAL SOCIAL WORK

MYRON E. WEGMAN, M.D., *Contributing Editor*

THE HANDICAPPED CHILD

By EUNICE W. WILSON
Boston

The term "handicapped child" tends to put emphasis upon the handicap rather than the child. There is still undue emphasis in many types of physical disability upon how a specific handicap can be overcome by special education or training methods, without sufficient attention to whether the child is having the normal relationships and social experiences necessary to equip him later to compete in adult society. If the ultimate goal for the child who is handicapped is participation with nonhandicapped children in normal life situations, the total needs of the child, as well as those for his specific handicap, must be considered.

This discussion portrays a method which individualizes a child and his needs in order to facilitate his social adjustment. Although the principles expressed have been drawn from experience with preschool children, they are applicable to some extent to all age groups. It is recognized, however, that problems arising in school age and adolescence may require different or additional types of service.

The reaction of parents to knowledge of a child's handicap is of great significance in the child's adjustment. The following reactions seem fairly general:

1. The basic parent-child relationship is somewhat threatened and feelings about the child may undergo change. Parents see themselves thwarted in their desire to rear a child in whom they can have pride and satisfaction. Their child cannot be compared on equal terms with the healthy normal children of their friends.

2. Parents feel conspicuous, especially if the handicap is obvious. They are self conscious about attention directed to themselves which results from sympathy or curiosity about the child.

3. Parents are sensitive and concerned as to whether the child will be accepted by other children and by other parents as a desirable companion for their children.

4. Parents may feel guilty or to blame for the child's condition. This is noted particularly in parents who have children with congenital defects or impairment from injuries acquired in unsupervised play.

There are also general ways by which parents attempt to overcome these reactions.

1. By acceptance of the handicap, emotionally, as well as intellectually and by taking

---

Mrs. Wilson is Director of Social Service, Massachusetts Eye and Ear Infirmary, Boston, Mass.
This study was supported in part by the Foundation for Vision.
Condensation of a paper read before the National Conference of Social Workers, Cleveland, Ohio, June 16, 1949.

constructive action in regard to it. This, of course, is the ideal way. The parents who are truly accepting can concentrate upon the child rather than his handicap. They do not dwell upon how the handicap affects the parent, but rather upon how it affects the child and how he can be helped to meet it in terms of his own life satisfaction rather than in terms of the parents' desires for the child.

2. By denial of the handicap. This reaction is seen in parents who insist that the handicap is only of a temporary nature. They seek one medical opinion after another, looking for a cure or a miracle, meantime delaying any positive action in relation to meeting the realistic situation.

3. By withdrawal of the child from his social environment. They may seek placement for him outside of the home or protect him from ordinary social contacts which they fear will be painful to the child or to themselves.

If the goal for the handicapped child is participation in normal society, one may question whether denying the handicap and withdrawing the child from society are constructive mechanisms for the child's life preparation. How can the child make progress in overcoming his disability or gain experience in establishing friends and meeting competition with nonhandicapped individuals if his social experence is limited largely to those with similar handicaps? Professional workers who are convinced that handicapped children have a place in normal society can often help parents to move from despair and inactivity to satisfaction and activity which will benefit the child.

Dr. David Levy has pointed out, "It is generally accepted that the most potent of all influences on social behavior is derived from primary social experiences with the mother."[1] Therefore, the mother's attitude toward the child is of particular significance. Her ability to love the child, to bear his disability and to derive maternal satisfaction from him does much to alleviate the anxieties and tensions of the father and other members of the family which may center around the child.

The problems which face the mother are real. A severely handicapped child places heavy demands upon her physically, emotionally and often financially. Although some mothers are under less pressure than others, physically and financially, all experience the emotional strain which comes from the excessive dependence of the child and his inability to participate freely with normal children. The child may require more attention than the mother has time to give with her household responsibilities. She is constantly confronted with his inability to do things for himself without slow and patient training. She may be frustrated in her attempts to relieve herself of his care for even short periods of time and in desperation seek placement outside of the home.

Knowledge of the detrimental effects of institutional life on young children is widespread. Therefore, every effort should be made for children to remain with their mothers or with a warm mother figure during their early years of life when they are establishing the roots of mature personalities.[2] Most parents have a real desire to keep their children with them and can do so if they are given confidence in their ability to provide the child with adequate care and attention.

Parents who are anxious seek advice. They are accustomed to turning to their pediatricians for information on all types of questions and problems which arise about their children. With the handicapped child they will even more readily seek his opinion and often rely fully upon his advice. Therefore, he is in an influential position to guide parents in the most satisfactory plan for the young child.

Consulting pediatricians have worked with the ophthalmologists and social workers at the Massachusetts Eye and Ear Infirmary in attempting to carry out a treatment program for over 200 young children blind from retrolental fibroplasia. This program aims to consider the basic needs of handicapped children and has been guided by the following principles:

1. Each handicapped child is an individual; his particular needs as a child should be studied and services offered accordingly.
2. Parental attitudes vary with individuals and must be taken into consideration if the child is to make a successful adjustment to his handicap.
3. In general, children find their greatest sense of security within their own family group; therefore, the handicapped child will usually find his greatest security there also.
4. Community services, which are useful to all children, such as child guidance clinics, nursery schools and foster care, should be available to handicapped children also.
5. Segregation, on the basis of the handicap alone, should be avoided.
6. Complete evaluation of the handicapped child physically, mentally, emotionally and socially is desirable for effective social planning.

The services offered, in carrying out these principles, have included medical social case work with parents which is directed toward the development of a warm and accepting parent-child relationship. While the parents have shown attitudes of rejection and over-protection in varying degrees, a continual attempt has been made to bring out their positive feelings of affection for the child. The ophthalmologists and consulting pediatricians have been key figures upon whom the parents have relied during their period of adjustment, not only for medical advice, but also for encouragement, realistic reassurance and moral support.

In our experience, we have discussed with the parents the fact that they are faced with a responsibility which will make greater demands upon them and which will necessitate more effort and adjustment on their part than is necessary with the normal child. We have tried, however, to help them face the total situation, gradually meeting problems one by one, rather than trying to help them settle the child's whole future in one or two interviews. It is characteristic of many parents to desire knowledge of all resources for the blind as soon as the child's blindness has been discovered, even to inquire during the child's infancy how he will be educated. When parents inquire very early about education they are told of the available resources but are also told that many factors will be taken into consideration before a final school plan is made and that definite plans can be delayed until the child is more nearly approaching school age. Factual information about other resources and literature on the blind are given on request but the parents' ability to use them is quite restricted until they have become somewhat adjusted emotionally. This requires time in all cases and, in instances where the mother is excessively disturbed, skilled treatment may be indicated.

The questions which are raised repeatedly in regard to the young blind child are the cause of his mannerisms, e.g., head banging and body swaying; whether he is normal mentally; how he can be stimulated to sit up, play with toys and be toilet trained; the best method of introducing the change from soft to solid foods; when he should participate in groups with other children; what accomplishments are necessary before he enters school, etc. Some of these questions could be asked about any handicapped child and are evidences of what might be considered normal anxiety in parents. The problems are

often accentuated in the blind child, however, because of his inability to learn through imitation, and his teaching and learning thus must become a more conscious process.

There is general awareness by our doctors that some of the mothers will need assistance of various kinds in order to care for the child at home. Therefore, the services of a preschool teacher, as well as a social case worker, are available from the hospital. These professional workers offer parents both consistent support and practical assistance. The teacher is available for consultation on training problems as they arise and for evaluation of the child's general development and readiness for group experiences. The case worker, in addition to dealing with the mother's adjustment, makes practical plans to relieve the mother physically and emotionally when the demands upon her become too great.

Since no valid objective psychologic tests for the blind child under school age have been developed as yet, parents are encouraged to refrain from seeking a mental evaluation before the child is 5 or 6 years of age. The possibility of the double handicap of mental retardation and blindness is a tremendous threat to the mother's ability to give of herself to the child. The mothers are encouraged, therefore, to develop the child to his maximum capacity in order that he may be able to perform at the level of his best ability when he is old enough to be tested. Mothers are given repeated approval for the progress which the children show as a result of their efforts.

The blind child, as well as the child with vision, may have emotional problems. There is little in the literature, however, about the emotional life of the young blind child and in our community there have been no resources available for their treatment, until very recently. Interest, by psychiatrists dealing with children, has now been stimulated and several children have received treatment and some study is under way as to what psychiatry can offer the blind children who are obviously disturbed.

In line with our principle regarding the association of handicapped children with normal children, a considerable number of the children have participated successfully in preschool groups with sighted children in their local communities. The teachers, as well as the children, have found the experience a satisfactory one. From the child's adaptation in the preschool situation, clues can be obtained as to factors which will influence a formal school plan when the child reaches 6 or 7 years of age.

On two occasions, as part of our study plan to determine ways to meet the needs of the parents, a group educational program was planned for mothers and their children. This was held as a residential course, in collaboration with a school for the blind,* with approximately 20 mothers and their children in attendance, for 2 weeks and 10 days, respectively. Emphasis was on parent education. Speakers were invited to discuss the normal child and his growth and development, although consultants who had had experience with blind children were in residence to help the mothers apply the concepts of the speakers to their individual child in relation to his blindness.

We found from this experience, as have others dealing with group counseling with parents, some benefits:

1. A sense of unity in the group secured from the feeling that the parents had a common problem.

2. A satisfaction derived from sharing experiences and gaining knowledge from each other.

3. A sense of encouragement from the fact that specialists in the fields of medicine,

* Perkins Institution and Massachusetts School for the Blind.

psychiatry, social work, child training and the blind were making a definite effort to help them.

We found also, however, that the parents who were able to participate in these projects were the ones who were most accepting of the blindness. The most disturbed mothers were not able to join the group. We also found that while most of the mothers seemed to obtain a considerable lift in spirits during the school period that this was not sustained for any great length of time. As they returned home and were confronted with their daily responsibilities and as new problems arose, they needed continued service of an individual nature. In other words, in most cases it was a helpful experience but it did not solve the mothers' problems in any permanent way and was not sufficient in and of itself.

Our experience with the blind child has been used as an illustration of an approach which may be applied toward the adjustment of handicapped children. Regardless of the type of disability, the basic problems of all handicapped children and their parents are similar. The element of dependency which is created by a handicap is a major problem which affects not only the patient but his entire family. Meeting and overcoming this dependence is the great challenge around which a treatment program is centered. In most cases it involves a variety of skills, medical, psychologic, educational, psychiatric and social. While all these services may be available only in large clinic centers, the principles set forth can frequently be met to a large extent by the pediatrician in charge of the child. Once parents can see possibilities for the child and are relieved of anxiety about his mental capacity and their ability to teach him, they show amazing resourcefulness in carrying out a constructive program for the child. The warmth and interest of professional people in whom they have confidence is one of the major assets in their success.

References

1. Levy, D., Maternal Overprotection, New York, Columbia University Press, 1943.
2. Bender, Lauretta, Infants Reared in Institutions, Bull. Child Welfare League of America, Inc. **24** (no. 7):1, 1945.

SPECIAL REVIEWS

JOSEPH STOKES, JR., M.D., *Editor*

THYMIC FUNCTION AND LEUKEMIA

By VAUGHAN P. SIMMONS, M.D.
Wauwatosa, Wis.

The thymus remains today in the minds of most people as "the enigmatic organ." Since the time of Galen, theories as to its nature and function have been set down but papers are still being written stating that the function of the thymus remains as mysterious as ever. From the middle of the 19th century until about 1920, a great deal of work was done to clarify its development and comparative anatomy and in the search for an endocrine function; since that time comparatively little has been done. Beard (1902)[1] bemoaned the status of the organ when he said: "And, indeed, has it yet fallen to the lot of any writer upon the thymus, to write the truth and to be believed? ! !" Doubtlessly, the reason for this lies in the great wealth of contradictory material found in the literature. There has scarcely been a claim made that has not been refuted by a number of subsequent writers. However, practically all students of the thymus are in agreement that the thymus produces lymphocytes; a great many have described the appearance of cells migrating from the thymus and filling the adjacent veins and lymphatics. In spite of this, there are few, if any, hematologists today who believe that the thymus is a significant producer of leukocytes. The present concepts often show the influence of a rigidly interpreted germ layer theory which held that blood elements could not arise from entoderm and consequently maintained that lymphocytes migrated into the gland at an early stage in its development and there reproduced themselves to build up its cortex. Beard[1] reviewed the early work in this field and presented his own studies on the thymus of the smooth skate. He pointed out that Kölliker was the first to describe the origin of the thymus from the epithelium of a gill pouch and at the same time gave an account of the transformation of the epithelial cells into leukocytes. This was verified by Prenant, Oscar Schultze and Beard himself. Opposed to Kölliker's discovery, Beard says that Stieda and His set forth the supposition, unsupported by proof, that the leukocytes had migrated into the gland from the exterior, possibly from the mesoblast. Quoting Beard, "In his work on the thymus Stieda asks '. . . how can adenoid tissue arise from an epithelium?' This is a matter for observation, and it may not simply be denied out of existence by a mark of interrogation!" Beard continues, "The difficulty may have been a real one in 1881, when there were no observations whatever—even after the publication of Stieda's own researches—beyond Kölliker's discredited but correct ones, concerning the origin of lymphoid cells . . . now there is no longer any difficulty about the matter, when dozens of drawings and thousands of preparations can be produced to show it. Where Nature places no obstacle in the way of carrying out a process, it is not for man to invent one! The fact is that in nature, as Kölliker first stated in 1879, adenoid tissue does arise from

(Received for publication April 11, 1949).

epithelial cells. Stieda's hypothetical views as to the history of the histogenesis of the thymus have been received by the majority of embryologists as though a basis of fact underlay them. Even today in most of the leading textbooks these views will be found gravely stated as the results of exact research." Maurer, who had earlier accepted Stieda's views, reversed his standpoint in 1899 after a number of years of research in favor of that of Kölliker but still hesitantly thought that the leukocytes had a mesenchymal origin in amphibians. Beard cited Gulland's work as showing that the first leukocytes in the body are found in the mesoblast in the neighborhood of the thymus and from his own work concluded that the first leukocytes in the body are formed in the thymus from its epithelial cells and, as such, must be regarded as the parent source of all the leukocytes in the body.

Bell,[2] using pig embryos, declared that he had never seen lymphocytes outside the thymus when there were none inside it but that they appeared outside shortly after they were formed there. At the stage when he was first able to see lymphocytes in the thymus there were none in the connective tissue around it or in the blood and he described lymphocytes as constantly being formed at the expense of the growing epithelial syncytium. He described also the presence of a great many erythroblasts in the thymic cortex. Badertscher[3] described the free erythrocytes of the interlobular septa as being derived from the lymphocytes present there. He also pointed out that Prymac and Schaffer both noted the formation of red cells from the leukocytes and that Maximow noted all transitions from lymphocytes to erythrocytes in the interlobular septa. Hammar[4] cited his own work and that of Maximow and Dantschakoff as indicating that the lymphocytes infiltrate the thymus from the outside; their evidence for this is not impressive. Ewing[5] cited Shaeffer as having observed many plasma cells derived from the lymphocytes (which has been frequently reported elsewhere also) and Maximow as noting eosinophils and mast cells. Harland[6] described mast cells forming in the thymus of the rat.

Hammar[4] noted that in inanition the picture in the thymus was that of an extensive mobilization and export of the lymphocytes of the organ with large numbers of these cells in its lymphatics and veins. He also noted that the medulla became richer in lymphocytes but no special significance was attached to this finding. He observed, too, that after roentgen irradiation there was chiefly a disintegration of lymphocytes instead of an emigration, noted even during the first two or three hours following the exposure. The reticular cells were more resistant and "Here, too, a reconstitution of the organ is brought about in the course of time, and here it is easier to follow the conditions of the reappearing lymphocytes than after inanition involution; they seem to appear first in the medulla, probably from its vessels, and from there they spread over the whole parenchyma."

Baillif[7] recently produced marked thymic involution in the albino rat with various colloidal substances (chlorazol black E, mercuric sulfide). The evolution apparently took place by pycnosis followed by karyorrhexis and complete cytolysis. Thymic epithelial cells are noted to hypertrophy, free themselves from their attachments and become either thymic lymphocytes or phagocytes which take up the injected material. "A small proportion of the original thymic lymphocytes escape destruction during involution, but it is only after the new lymphocyte population has been largely restored that mitotic figures are frequently observed in this type of cell. It is thus believed that most of the new lymphocytes arise through transformation of epithelial cells."

A recent report by Murray and Stout[8] on tissue cultures from human adult thymi re-

moved at operation from five patients, three of whom had myasthenic symptoms, indicated that the "thymocytes appeared to be closely related to the epithelium in origin."

From the evidence so far presented, one is led to believe that the basic concepts that governed the thinking of many of the early workers on the thymus were incorrect. The supposition that epithelial cells cannot turn into lymphocytes can no longer merit credence but the fact remains that much of the basic literature on the thymus was written under the influence of this dogma, as it appears to have been in the early part of this century. Authors who would not grant that the thymic lymphocytes could arise from the medullary epithelial cells were forced to the conclusion that these cells must be migrating into the organ, hence Hammar's statement previously quoted, that the lymphocytes appeared first in the medulla "probably from its vessels." Whenever a leukocyte has been described in diapedesis through a vessel wall, it has been said that it was coming into the thymus. Even the relatively current literature which describes the histologic appearance of the thymus in leukemia portrays the cells at the margins of the lobules and in the interlobular septa as "infiltrating into the involuted thymus." Such appearances as this can be seen in the thymi from normal mature female guinea pigs during the luteal phase of the estrus cycle; here, correlations with other stages of the cycle make it obvious that these cells are leaving the organ and not entering it (author's unpublished work).

Kindred[9] made a number of studies on the quantitative aspects of hemopoiesis by various blood-forming organs including the thymus which give the latter organ greater stature than it can be given by qualitative descriptions alone. By comparing mitotic rates and cell destruction with unit volumes of the different tissues and correlating this with the numbers and types of white cells in the blood, he made calculations indicating the activity necessary in each organ to maintain itself and to produce an excess of cells for peripheral distribution. In his 1940 paper, his data from 15 day old and 20 day old albino rats indicated that the thymus in these animals was "the only organ which is producing small lymphocytes in excess of local needs. . . . It can be seen that this excess is quite sufficient to meet the demands of growth of the lymph nodes of the body even if the mitotic cycles of the thymic cells are calculated to be of 3 hours duration." He pointed out that "According to Yoffey, 250,000,000 small lymphocytes enter the blood via the thoracic duct in a 10 kg. dog every hour. Furthermore, Yoffey and Drinker from a study of the rate at which lymphocytes enter lymphatic vessels from the periphery of the body (one for every 30 in the thoracic duct) conclude that the lymphocytes entering the blood stream via the thoracic duct must come from organs which drain into it and not from the peripheral lymphatics. The further fact remains that these lymphocytes which enter the thoracic duct must come from organs which have a good lymphatic drainage. This at once rules out the spleen and the bone marrow, but permits the inclusion of the thymus, which according to Severeaunu and Matsunaga has a rich lymphatic supply which permeates all parts of the organ. The lymph nodes can be included too, but the data given in the present investigation show that these organs are not producing excess lymphocytes at this time. The view that the thymus may be the source of the lymphocytes collected by Yoffey is further supported by a contrast between his counts of the numbers of small lymphocytes entering the blood stream via the thoracic duct and the present figures on the production of small lymphocytes by the thymus. According to his data, the equivalent of 20.0% of the total lymphocyte population of the blood is entering the blood stream every hour via the thoracic duct. The present results show that the production of small lymphocytes by the thymus is

equivalent to about 20.0% of the small lymphocyte population of the blood if the mitotic cycle of the thymic cells is reckoned as of 1 hour in length. It is reduced if the mitotic cycle is longer. The present figures show that these small lymphocytes are needed by growing lymph nodes and lymphoid tissue in these early stages, whereas Yoffey speculates that they may be filtered out in the bone marrow to be used as ancestors of the blood cells as Jordan and Spiegel suggested and as Jordan has held for the adult from his studies of the avian bone marrow. These figures suggest that the thymus may be of much more importance in the early stages of development of the lymphoid organs of the body than has been suspected." Additional data on this point in 80 day old rats is given in Kindred's 1942 paper[10] as well as quantitative evidence to support Jordan's views that the erythroid population of the bone marrow must receive some outside source in order to produce sufficient red corpuscles to meet the demands of the body.

Andreasen[11] reported a study on the lymphocytopoietic activity of the thymus, lymph nodes and spleen of male and female mice 2 months of age. He found the ratio of mitoses to nondividing nuclei to be about 0.3% in the thymus, 0.06% in the lymph nodes and 0.02% in the spleen. "These results correspond with observations made in the rat in which the significance of the thymus as a lymphocyte producing organ was previously demonstrated." (The same author reported in 1947[12] that the thymic "lymphocytes are formed in the cortex, where they remain but a very short time and then they enter the blood stream by way of the capillaries or lymphatics.")

Ghika, cited by Major,[13] concluded that the thymus is primarily a hemopoietic organ and forms leukocytes but probably no erythrocytes.

Most workers have reported a transient leukopenia after thymectomy; some have reported a permanent reduction.

Hammar's[4] observation of thymic lymphatic vessels and veins filled with lymphocytes during the involution of inanition, Christensen and Griffith's[14] observation of migration of lymphocytes from the thymus and their "paradox" that "The common occurrence of mitoses of both lymphocytes and reticular cells while the gland as a whole was undergoing regression seems to be a paradox of involution," and the observation by Dudgeon[15] of a thick sterile fluid, resembling pus but composed almost entirely of lymphocytes, as a normal feature in the interior of large thymus glands, together with the evidence already given and more that will be cited later, should leave little doubt about the ability of the thymus to produce and distribute white blood cells.

Renaut (1897)[16] described the collecting lymphatics of the thymus and Severeaunu (1909)[17] reviewed the literature on thymic lymphatics to that time and described his own work. Recently, Cowdry[18] commented in his histology text that "Thymic nodules, in common with Malpighian bodies of the spleen, have no afferent lymphatic vessels of any kind." This should make it clear that any lymphatics seen in the thymic interlobular septa that are filled with cells are carrying them away from the thymus and not into it.

A number of conditions in which there is a leukocytosis are definitely known to have a concurrent atrophy of the thymus. The work of Selye (1936[19] and numerous subsequent papers) has shown a number of stimuli which evoke the "alarm reaction," part of which is thymic atrophy and adrenal hypertrophy. Other authors who have done leukocyte counts in the same conditions described as causing an alarm reaction have reported an early leukocytosis. Farris[20] studied the peripheral blood in humans under different emotional stresses and found a relative lymphocytosis within five minutes after onset of the stimula-

tion; in his work on the rat, he was able to substantiate the work of Martin[21] indicating that muscular and mental activity increased the total leukocyte count. Adrenalectomy prevented the leukocytosis in the rats. Farris and others believe that the contraction of the spleen plays a major role in the outpouring of cells. Martin observed a human case after splenectomy and found no difference in his responses to stimulation; he thought the lymph glands were chiefly responsible for the increases for they contract under the influence of adrenaline and also that the increased blood flow due to the cardiac stimulation by adrenaline causes the granular cells to be washed out of the bone marrow. The thymus seems not to have been considered. Garrey and Bryan[22] cited examples of leukocytosis after running and other exercise; they mentioned one author (Raisky) as ruling the spleen out of the picture as a significant source of the leukocytes because the white cells continue to increase after the maximum increase in red cells has taken place. Garrey and Butler were also described as having obtained an activity leukocytosis after splenectomy. It was pointed out that there is a marked increase in thoracic duct lymph flow after adrenaline and that lymph is the chief source of blood lymphocytes (see Kindred's work). The migration of lymphocytes in inanition and acute infections has been noted by many authors (see Crotti[23]).

The fact that many of the thymic lymphocytes undergo a rather sudden change in form from lymphocytes to myelocytes during the period of function of the corpus luteum after follicular activity in the guinea pig (author's unpublished work) strongly suggests that they may be under hormonal control. There is also good indirect evidence for this reflected in the peripheral blood picture of normal humans. While the literature seems to be inconclusive as far as adults are concerned, the picture is clearer in infants.

It is well known that at birth the uterus and vagina of the newborn show marked growth changes that last only a short time before regressing. Paton and Goodall (1904)[24] demonstrated experimentally in the guinea pig that there is a sharp drop in the weight of the thymus after birth. Garrey and Bryan[22] quoted numerous authors who have described a leukocytosis after birth which is primarily due to single and double lobed polymorphonuclear neutrophils with trilobed forms appearing about the ninth day to two weeks. "By the end of the second week lymphocytes are present in excess as they are throughout infancy." Warfield (1902)[25] did counts on 10 newborn infants before they had received any nourishment and then on the 3rd and 11th days of life. He found that the leukocytes were more numerous on the day of birth than at any other time of normal life. The percentage of large mononuclears and transitional cells was nearly the same as that of adults. Polymorphonuclears were found to be relatively and absolutely increased. By the end of the 11th day the differential count was practically the same as that given in textbooks as normal for the infant's blood. I would like to suggest that these blood cell changes are under hormonal control just as has been ascribed to the uterine and vaginal changes.

PERSISTENCE AND INVOLUTION OF THYMUS

There is normally a large amount of thymus tissue remaining after puberty. Hammar[4] spent a great many years in the study of the thymus and made numerous valuable contributions to our knowledge of its development and comparative anatomy as well as its appearance in health and disease in human cases of whose histories he was cognizant. He stated in 1921: "No idea about the thymus has perhaps been more widespread and more generally adopted than that the organ is of a transitory nature, that at a certain early age it begins to decline and soon disappears, or at least ceases to function. It is true that the

views as to the time both for the beginning of the regression and the disappearance of the organ have varied to a very great extent. The opinion already upheld by Galenus, that the turning point in the existence of the organ is at birth, has still followers in this century. Sometimes writers have even wished to assign the entire activity of the organ to embryonal life and assumed that it was spent soon after birth. The most general view during the latter part of last century held, however, that the highest point of the development of the organ was during earliest childhood, 1 to 2 years; opinions were very much divided as to how soon and to what extent the organ atrophied after this time. When in exceptional cases a large thymus was found after the time when it was considered that the thymus would normally have been involved, it was called a 'persistence' of the organ, or, later on in such cases, when it was considered that the organ had already been atrophied and had again grown and begun to function once more, a 'revivescence.'

"In the form indicated here the old theory of an 'age involution' of the thymus was certainly incorrect."

He called attention to the fact that anatomists before 1890 had noted the existence of a thymic fat body with considerable parenchymal remains during old age and stated further that "the organ is a factor to be reckoned with throughout life, and not only during childhood." Crotti,[23] too, cited the experiences of Sappey and Waldeyer who "after very careful dissections of fresh cadavers, came to the conclusion that there is no such thing as total disappearance of the thymus even in old age. They found in cadavers of patients of from 60 to 80 years old that there is always present in the mediastinal space a fatty mass of peculiar consistency and coloration, containing without any doubt remains of thymic parenchyma. Mitotic figures are also present, showing that the regenerating power of the parenchyma is still present. They consequently consider that the thymus function is never really suppressed during life and they furthermore claim in accord with Hammar and Lampe, that the words *persistence* or *revivescence* of the thymus are misnomers. It is as erroneous to speak of the persistence or revivescence of the thymus as if one were to speak of the persistence or revivescence of the breast, kidney, or ovary. So, in conclusion, we may say that the thymus increases in weight up to the time of puberty, namely, between the 10th and 15th years, that during this time it reaches its maximum of development, and that it then begins to undergo a physiological involution but never disappears entirely during life." The finding of thymic tissues at autopsies of individuals of all ages has been confirmed by numerous other investigators and appears to be definitely established. Boyd[26] gave the following data on thymic weights: "Beginning with an average weight of 13 grams at birth, the thymus increases to an average weight of 35 grams at puberty, then atrophies to 15 grams by the age of 50." It is stated in addition that the thymus is usually largest when the death is sudden from any cause. (One should keep in mind when reading weights of thymic tissue that the interlobular fat is included in this measurement and that without histologic or chemical control the figures may be misleading. It is unfortunate indeed that much of the literature on the thymus has been based on weights alone, especially the clinical literature.) Neste[27] frequently found at post mortem of soldiers who had committed suicide a "hyperplasia" of the thymus and lymph glands together with atrophy of the adrenals. Groll, cited by Falta,[28] using bodies of soldiers killed in World War I found that the persistence of the thymus gland is much more common than it is ordinarily thought to be. Hellman, cited in the same volume, also made the same observation for the lymphatic tissue in general for both rabbits and man. Richter,[29] referring to the

"hyperplasia" of the lymphatic system in war victims, considered it a normal finding and expressed himself emphatically in this regard: "Der Status thymicus sollte endlich dorthin geworfen werden, wohin er seit langem gehört und wohin ich ihn seit Jahren verwiesen habe, nämlich ins alte Eisen; aber ein Irrtum ist schewerer zu bekämpfen als hundert Wahrheiten."

Numerous observations have been made on the "persistence" of thymic tissue in lower animals. Fulci, quoted by Park and McClure,[30] gave figures showing the frequency with which the thymus exists unatrophied in adult animals. Farris and Yeakle[31] removed thymus remnants from rats 553 to 1058 days old and found little variation in organ weight and the tissue resembled the thymus that has undergone severe accidental involution in a younger animal. Microscopically, they found concentric Hassall's corpuscles and lymphocytes. Fenger[32] used beef fetuses, calves, full grown cattle, adult hogs and sheep of all ages and noted the size and composition of the gland. He concluded: ". . . it is reasonable to assume that this gland does not cease its systemic activity throughout the growing and reproductive periods of the life of these animals." He also noted that "adult cattle and sheep (herbivora) contain more thymus tissue per unit of body weight than adult hogs (omnivora)." Bürker[33] thought that the vegetarian and carbohydrate diet may have had something to do with the persistent thymus glands found in front line soldiers. Their state of sexual activity must be taken in consideration also. Hammett[34] stated that "a study of thymus growth in the albino rat under close to ideal conditions with respect to diet, environment and health, shows that there is no such phenomenon as the 'age involution of the thymus' up to the time of young adulthood, some time after puberty." Hammar[35] contested this statement because Hammett did not make histologic observations and attributed the weight increase found by the latter to an increase in amount of interstitial tissue. This was not proved. Crotti[23] stated that physiological involution takes place in cattle starting with the fourth to fifth year but is never completed, in the cat from the second to third year and also in the horse after the second or third year. None of these writers considered the state of sexual activity of the experimental animals or humans.

The task of assigning a particular time in life when the thymus atrophies has been complicated by the phenomenon of so-called "accidental involution" by supposed nonphysiologic stimuli, as compared with the involution that is assumed to take place physiologically at some set time which varies as accepted by numerous authors previously outlined. It was pointed out by Wharton, cited by Hammar,[4] as early as 1659 that the size and structure of the thymus and the general condition of the organism were related. Selye[19] has published numerous accounts of diverse stimuli which cause adrenal hypertrophy and atrophy of the thymus which takes place in a short time ("alarm reaction"). This involution is said to take place chiefly by a destructive influence on the cells in situ. In many other cases, however, the involution has been attributed to a decrease in the number of cells present in the cortex, not by a destructive process but by an emigration of cells. Christensen and Griffith[14] studied the involution and regeneration of the thymus in rats fed choline deficient diets and noted: "Migration of lymphocytes from the thymus appeared to be the most important process in involution. No other single process apparent could produce such rapid reduction in size and such extensive loss of lymphocytes without definite cytological changes. The disappearance of lymphocytes resulted both in thinning of the cortex in partially involuted glands and in complete loss of the cortex in the glands which had undergone the most extensive involution." These authors also noted the

apparent transformation of the thymic lymphocytes at the periphery of the lobules into monocytes, plasma cells and probably connective tissue cells; they also observed a change in the cells from their characteristic basophilia to complete eosinophilia while retaining their cell outlines. Smith and Wilson[36] studied the effect of choline deficient diets on the thymus in mice and found little change, concluding that the thymus of the albino mouse was much more resistant to choline deficiency than that of the rat. Numerous investigators have noted the effects of inanition on the thymus. Friedleben, quoted by Morgulis,[37] noted in fasting dogs that the reduction in size of the organ was considerably greater than that of the entire body or that of any other glandular organ. Hammar also noted the reduction of thymus size through inanition. He reported, "The reduction of the cortex is chiefly brought about by a wholesale emigration of lymphocytes from it. Normally it is principally the septa between the cortical follicles that appear to be infiltrated by leukocytic forms, and among these there are certainly always lymphocytes, but these are mixed with and often exceeded in number, by larger forms—among others, eosinophile myelocytes and plasma cells (Shaffer). Now under the influence of hunger all the part of the interstitium adjacent to the parenchyma is flooded with lymphocytes; the larger forms of leukocytes withdraw, sometimes apparently disappearing altogether. At the same time lymphocytes are found in large quantities in the lymph vessels and veins situated here. The medulla, too, becomes richer in lymphocytes. Everything points to an extensive mobilization and considerable export of the lymphocytes of the organ." Jonson[38] studied the effects of inanition on the thymus in young dogs. One of his figures is reproduced here (Fig. 1) to show the striking results obtained by undernourishment and the remarkable regeneration after an adequate feeding regime was re-established. The weights of the organs are indicated as well as the duration of the periods of inanition and feeding. Even in extreme stages of involution the process is reversible and the parenchyma is rapidly reconstituted under the influence of an abundant supply of nutriment to the animal. The involution took place both by a degeneration and emigration of lymphocytes. Hammar[4] said: "The stages in this reconstruction process are on the whole the same as in the embryological development, first a diffuse lymphocyte infiltration, followed closely by a central medullary differentiation and finally a reappearance of Hassall's corpuscles in the medulla." He also quoted Fulci as noting thymic atrophy during pregnancy and subsequent regeneration; this has also been reported by others. Hammar and others have also noted the involution of infection to take place chiefly by an emigration of lymphocytes and only in exceptional cases by disintegration of these cells in loco; regeneration occurs the same as after the involution of inanition. Andersen[39] described thymic atrophy in rats 40 hours after the end of exercise which could not be correlated with significant histologic changes except slight decrease in the width of the zone of thymocytes. Many investigators have studied the effects of hormones on the thymus. Hammar[35] and others have shown that the repeated injections of blood serum from sexually mature animals of the same species into prepubertal animals causes an involution of the thymus while such involution does not take place if the injections are made with blood serum from sexually immature animals. Castration has long been known to prevent involution of the thymus until much later in life and has been said by some to cause an actual hypertrophy; if carried out after puberty, a rapid regeneration has been described by many authors. Hammar[4] said: "It seems from this as if the effect of the castration is less that of checking the process of age involution than that of transferring the regular metabolic processes in the organ, perhaps its produc-

tion and elimination of lymphocytes especially, to another and higher plane than in the case of intact subjects of the same age." He cited also a case of his own showing that, even in man and even when carried out relatively late, postpubertal castration may have the same effect. A number of the earlier workers were skeptical about the powers of regeneration. Park and McClure[30] remarked about Fulci's work: "The histologic evidence favoring regeneration, brought forward by Fulci, is extremely strong, and we regret that it is

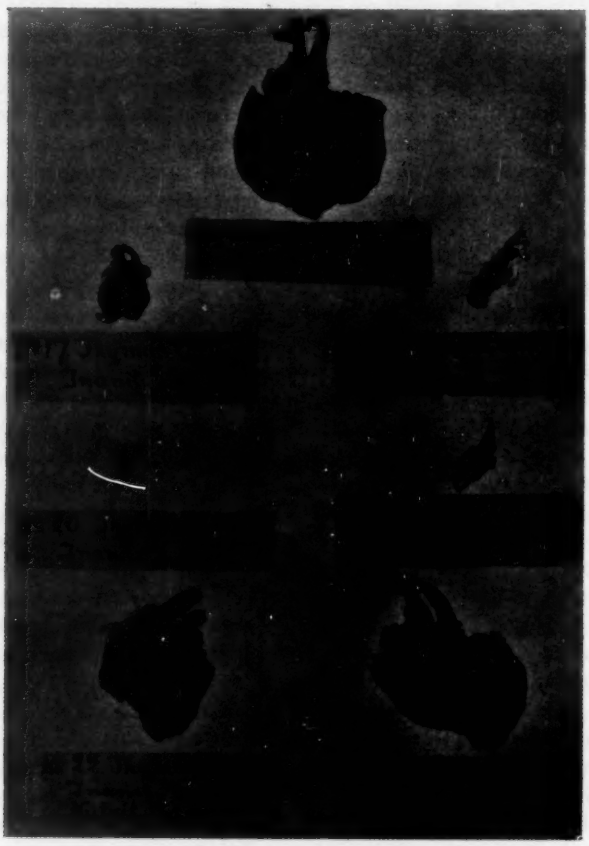


FIG. 1. Illustration of effect of inanition followed by adequate nutrition on thymus of dog. (After Jonson[28])

impossible to present it in detail. One observation which he made is, however, so far out of harmony with his interpretation of the significance of the changes in the rest that we cannot but wonder if the latter were truly regenerative in nature, namely, that in the majority of instances the histological alterations in the rest occurred in the same way and were the same in character irrespective of the age of the animals. Two of his dogs and all of his cats were 1 year or more old, and some of his rabbits were 3 years old, when partially thymectomized, and should have altogether outgrown dependence on thymic function." I feel sure that if Beard had read this latter statement he would have repeated his words

of 1902: "Where Nature places no obstacle in the way of carrying out a process, it is not for man to invent one!" The influence of Galen was a far-reaching one indeed!

Thymic hypertrophy has frequently been described also in Grave's disease, Addison's disease, acromegaly and myasthenia gravis. The adrenal steroids cause atrophy, as noted by Ingle[40] and many others. Dontigny[41] gave desoxycorticosterone acetate to adrenalectomized rats and found marked reduction in thymus weights but no effects on the weights of the lymph nodes; he cited Selye's work with DOCA also. Selye[19] had observed that the adrenals were apparently necessary for the thymus to undergo sudden involution. Marine[42] cited a number of references to show that prolonged feeding of dessicated thyroid has also been followed by enlargement of the adrenal cortex and that it is also enlarged during starvation. The inverse size relationship of thymus and adrenals are well known. Marine[43] cited evidence to show that adrenalectomy causes rapid degeneration in highly involuted glands, provided the thyroid is intact, and that thyroidectomy hastens involution in rabbits as well as preventing the regeneration which ordinarly follows adrenalectomy; thyroid feeding has been shown to cause thymic enlargement. Selye[19] showed too that "hypophysectomy produces only very slight thymus involution, if any, in the rat, and that the thymus of hypophysectomized animals does not undergo as marked accidental involution as that of normals." Numerous authors have described the effect of both male and female sex hormones on the thymus as causing an involution. The injection of gonadotropins causes an involution only so long as the sex organs are intact (Evans and Simpson[44]). Henderson[45] observed that "in bulls which had been used for serving cows, and in heifers which had been pregnant for several months, the thymus exhibited a much more marked atrophy than was the case with those which had not exercised the reproductive function." There seem to be no other specific studies to determine the effect of male sexual activity on the thymus; it should be investigated.

CLINICAL AND PATHOLOGIC CONSIDERATIONS IN LEUKEMIA

Involvement of the thymus in leukemia has frequently been noted. In reference to lymphoid leukemia, Moore[46] said, "In most cases of leukemia there is involution of the thymus, but the association of a tumor of the thymus and lymphoid leukemia has been reported too often to be considered coincidence," and refers the reader to a paper by Craver and MacComb.[47] Quoting the latter authors, "In a considerable series of cases a large sarcomatous tumor of the thymus with a leukemic blood picture has been the chief feature, so that leukemia with involvement of the thymus came to be recognized as an atypical and maligant variety. These growths have been designated by Orth as malignant leukemic lymphoma. As noted by Kaufmann, 'In leukemia, marked enlargement of the thymus is occasionally seen, especially in acute lymphatic leukemia.' The rapid growth of the thymus may be out of all proportion to the hyperplasia of other lymphatic structures and to the blood picture, thus giving rise to a mistaken diagnosis of thymoma as an entity. As stated by Heubner, 'with thymic tumors the other lesions of leukemia have not always been fully developed.' In 1925 Friedlander and Foote reported a case of 'malignant small-celled thymoma with acute lymphoid leukemia.' Here the unripe lymphoblasts of the blood stream so closely resembled the cells of the thymic tumor found at autopsy that the question arose—was the source of the abnormal cells of the blood an outbreak of the tumor through the wall of some vein, or was the whole process true lymphoid leukemia? This question was not definitely decided." They present a number of other reports of cases of leukemia with thymic tumors and four cases of their own of lymphatic leukemia with

thymic enlargement, concluding in part that: "(1) Tumefaction of the thymus in association with lymphatic leukemia, while rare, is a definitely recognized variant of that disease and is probably the result of leukemic infiltration of the organ. (2) In cases of thymic tumor the blood and lymph node system should be carefully observed for evidence of leukemia. (3) The thymic tumors associated with lymphatic leukemia are radiosensitive."

Crosby's[48] paper on malignant thymus tumors cited 103 references and listed the number of cases described to that date as 166, of which 122 were so-called sarcomas and 44 carcinomas. He states: "In both sarcoma and carcinoma of the thymus gland, the tissues in close approximation to the thymus are most often invaded. However, metastasis may take place to almost any tissue in the body." It is not stated whether a leukemic blood picture was present in cases of metastasis or otherwise.

Evans and Leucutia[49] discussed the neoplastic nature of lymphatic leukemia and its relation to lymphosarcoma. They refer to Palma who described in 1892 the transformation of a primary sarcoma of the thymus to lymphatic leukemia. The same transformation is said to have been described by many authors and it was considered only to be the accidental occurrence of two distinct lesions. Fabian was also cited as having reported several cases of thymoma (probably lymphosarcoma) showing the blood picture of typical lymphatic leukemia. In these authors' own three cases with the diagnosis of lymphosarcoma of the mediastinum made in two, the blood picture was normal in the beginning in each case but was characteristic for lymphatic leukemia "as soon as the bone marrow became involved by foci of lymphosarcoma."

Thorpe[50] reported "an unusual case of thymic hypertrophy" which was associated with acute leukemia in a white boy 6 years of age. Scott[51] reported in the same journal a case of lymphosarcoma of the mediastinum in a child in which there was no leukemic blood picture. At autopsy the diagnosis was "lymphosarcoma of the small round cell type, the origin probably in the thymus."

Margolis[52] studied a series of 32 cases of lymphatic leukemia which had come to necropsy at the Mayo Clinic. He quoted Ordway and Gorham as reporting in a consideration of lymphatic leukemia: "The thymus gland is usually large and may even show tumor-like nodules and infiltration of the surrounding tissue. Histologically, the change is comparable to that found in the lymph glands." Ewing, he said, remarked: "It is a notable fact that in most cases of leukemia and pseudoleukemia the thymus gland fails to participate in the process." He continued that Schridde was of essentially the same opinion and "expressed the belief that it has not been established in the literature that true thymic hyperplasia occurs in lymphatic leukemia. He was not able to observe more infiltration in the thymus gland than he observed in the skin, for example." Margolis himself, on the basis of accepted views at that time, stated: "On a priori grounds, it may be assumed that if the small thymic cells are true lymphocytes, having not only a morphologic resemblance to blood lymphocytes, but also a common histogenetic relationship to them, there would occur in lymphatic leukemia hyperplasia of the thymus gland step by step with hyperplasia of the lymphatic structures elsewhere in the body." In describing the appearance of the leukemic thymus glands, he states: "It is significant that the changes just described occurred as frequently in the glands of children as in those of adults, and in them the factor of involution from age had not yet come into play." I would like to quote his entire "Comment" on his paper which I consider as representative of current thinking on the subject:

"In the entire series of 32 cases of various types of lymphatic leukemia, enlargement of the thymus gland was found in only four cases. In the remaining 28 cases, the thymus gland either did not show notable abnormality or showed gross or histologic evidence of varying degrees of involution. That 10 of the cases were in children emphasizes the fact that the involution was not always that due to physiologic retrogression associated with age, but that it was a reaction of the thymus gland to the disease process. It is not possible, of course, to say just what influences the gland in leukemia. The altered nutritional state must be considered as one of the possible factors productive of the process of involution, since the relation of disturbed nutrition to pathologic involution of the thymus gland is now well established. What seems more interesting, however, is the striking involution of the thymus gland in a disease the essential feature of which is a tendency to hyperplasia of lymphoid tissues. This, indeed, brings into question the often quoted concept of the true lymphatic nature of the thymus gland and its small thymic cells. That the small thymic cells should react so unlike the lymphocytic elements elsewhere in the body suggests that they may be of inherently different nature, unless one postulates an overwhelming influence in leukemia productive of thymic involution and one sufficient to overcome the general stimulus to lymphoid hyperplasia. I have no reason to believe that the latter is the case. The more direct interpretation of a different biologic nature of the small thymic cells and the blood lymphocytes seems more reasonable. I have already quoted evidence that has been adduced by many observers pointing to the epithelial source of the small thymic cells. The reactions of the thymus gland in leukemia also indicate a biologic difference; hence a different histogenetic source of the thymic cells from that of the blood lymphocytes does not seem unlikely.

"The occurrence of an enlarged thymus gland in the four cases of leukemia would at first seem to militate against this hypothesis. However, the histologic features of these cases, too, point to an advanced degree of involution with secondary infiltration of the organ by lymphocytes. The lymphocytes in these glands appeared as densely aggregated in the connective tissue and capsule of the organ as in the parts normally occupied by the thymic parenchyma. Furthermore, the degree of infiltration in the thymus gland in the three cases of leukosarcoma paralleled that in other nonlymphatic organs, such as the kidney and the liver. It seems obvious from this that enlargement of the thymus gland in leukemia, when it does occur, represents merely a part of the tendency to infiltration of organs by lymphocytes that is so characteristic of this disease. In other words, the thymic enlargement in these cases does not represent true hyperplasia of the small thymic cells, but is due to nonspecific infiltration with lymphocytes, such as frequently affects the kidneys, liver, skin and other nonlymphatic structures in the body." Figure 2 is a reproduction from this article showing "evidence of involution and infiltration of interstitial tissue with lymphocytes." This picture is similar to that seen in many of my guinea pig thymus preparations where emigration is obviously taking place.

Cooke[53] reported on mediastinal tumors in acute leukemia and presented a clinical and roentgenologic study. Figure 3 is a reproduction of the author's Figure 3 (case 2) showing in "A" a mediastinal tumor in a 5 year old boy with stridor and cyanosis and in "B" the same child six days later showing the disappearance of the mediastinal shadow after roentgen therapy. This picture is used as being typical of a number of others given in this paper and elsewhere. Dr. Cooke stated: "The purpose of this paper is to report a group of

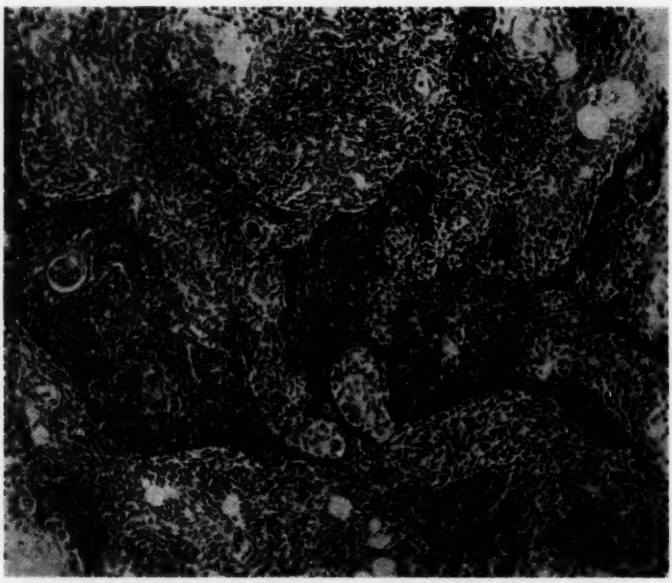


FIG. 2. "Section of thymus gland of a child, aged 6, who died of acute lymphatic leukemia. There is evidence of involution and infiltration of interstitial tissue with lymphocytes." (After Margolis[82])

nine cases of acute leukemia with large mediastinal tumors or infiltrations, and the results of roentgen therapy on this condition. While the occasional presence of such tumor masses in acute leukemia has been recognized, the lack of any but casual reference to them in standard texts indicates that they are considered rare. It is becoming increasingly evident, however, that a definite proportion of patients with acute leukemia have mediastinal masses which tend to give characteristic symptoms of pressure. These tumors may precede

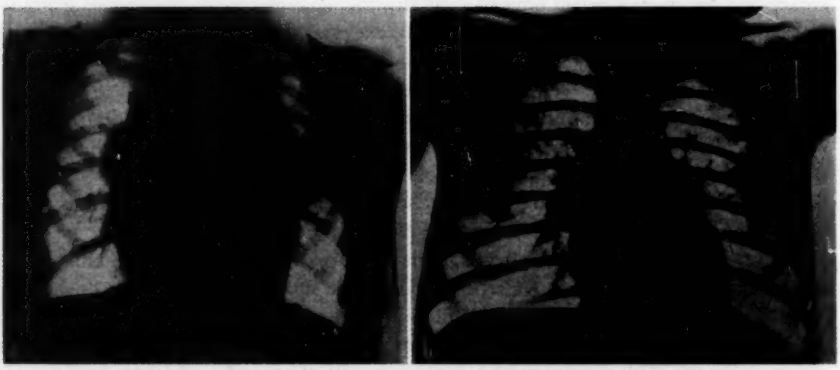


FIG. 3. "Roentgenograms showing A, mediastinal tumor in a 5 year old boy with stridor and cyanosis; B, six days later, disappearance of mediastinal shadow after roentgen therapy." (After Cooke[83])

the typical blood changes, and, in my observation, they have been the most common form of massive mediastinal enlargement in children.

"Localized tumor masses composed of round sarcoma-like cells have at times been observed at necropsy in patients dying of acute leukemia. These have been noted most frequently in the anterior mediastinum and have usually been considered of thymic origin, but have occurred less often in other locations, as, for example, the subcutaneous tissues, skin, bones and serous membranes. Sternberg, in 1905, designated the group of cases with localized lymphoid tumors and a leukemic blood picture as 'leukosarcoma,' because of his belief that they represented a true neoplastic tumor, and his view and term have met with rather wide acceptance. Such observers, however, as Naegeli and Fraenkel have felt that such tumor masses are only a part of the leukemia, and consider that they are comparable to the tumors found not infrequently in the cervical and other lymph nodes. Similar mediastinal tumors in patients without blood changes or other signs of acute leukemia have been called lymphosarcomas or thymomas. Most of these cannot be differentiated from leukemic tumors even by microscopic sections."

Further, "During the past few years several writers have recognized the mediastinal mass, especially by the use of the roentgen rays, and have treated it by irradiation. In certain of these patients the blood changes of acute leukemia have appeared some time after the appearance of the mediastinal tumor in a manner quite similar to that observed in several of the children whose cases are here reported." A number of cases from the literature are presented in which a mediastinal tumor was present and the author noted: "It is rather striking that almost all the authors who have reported such cases have considered the condition one of a true mediastinal neoplasm of the lymphosarcoma type, and that the acute leukemia resulted in some way from the primary new growth." In regard to the actual cells in the leukemia, "The character and origin of the abnormal nongranular cells present in the blood in acute leukemia is still in dispute. They have long been considered by many observers to be lymphocytes or lymphoblasts, and the common term 'acute lymphatic leukemia' expresses their presumably lymphoid origin. In recent years the view that such cells originate in the bone marrow and are more closely related to myeloblasts has been gaining favor. In addition to their morphologic resemblance, their biologic relationship is indicated by the demonstration (by myself) of the similarity of the proteolytic ferment content of the acute leukemic cells and the granular myeloid cells. Reference in this paper to these leukemic cells as lymphocytes follows the usual custom to avoid confusion, although they are probably myeloblasts." The cases of nine boys with massive leukemic enlargements of the thymic region are reported in this paper. The location of the mass is "constantly in the superior and anterior mediastinum, and, from the organs of the neck above, the tumor spreads down over the pericardium and often laterally in two wings. Its nodular arrangement as seen at necropsy is shown in the roentgenograms by rounded irregularities of the borders. In all instances the mass occupies the position in which the thymus is found in infancy and is of approximately the same shape, although this may be due to its moulding by the surrounding structures. The character of all the tumors examined at necropsy is similar. They consist of a fairly firm, gray, translucent, cellular tissue with a tendency to be arranged in lobules, adherent to the sternum and pericardium and at times to the structures at the base of the heart. The surrounding tissues are not grossly invaded in the manner of malignant neoplastic growths, although portions of the pleura are sometimes thickened by a similar infiltration.

The lymph nodes in the vicinity are often enlarged but not always, and are usually distinct from the main tumor, although sometimes imbedded in it. Microscopically, the cells composing the mass are mononuclear and indistinguishable from those present in the blood, which infiltrate the bone marrow, lymph nodes, spleen, liver and kidneys in such cases and also in cases of acute leukemia not accompanied by thoracic tumors. Mitotic figures are usually found, although this is also true of other leukemic infiltrations. At the edges of the mass the cells have a tendency to infiltrate the surrounding connective tissues, but not, as previously mentioned, by growth of considerable masses of cells into adjacent structures. It is rare that any remnants of thymic structure, such as either the small thymic cells or Hassall's corpuscles can be recognized, and it has been urged by Margolis that in leukemia the thymic cells undergo an involution and hypoplasia. The question of whether such leukemic mediastinal masses have their origin in the thymus gland is of some interest since thymic elements are absent. Mediastinal lymph nodes would seem to form the only other source of origin in this location, but the lobular character of the mass, its 'thymus-like' appearance, and its total lack of resemblance to enlarged nodes would seem to exclude this possibility. The previously mentioned tendency to occur in younger persons would also favor the assumption of a thymic origin because of the fact that thymic tissue tends to disappear in later life. It is probable, therefore, that such mediastinal enlargements originate in the thymus or its remnants even though characteristic thymic structures are not demonstrable. The fact that the mediastinal tumor has been present before the leukemic changes in the blood appeared in certain cases, as, for example, in four of those here reported, is of much interest. This has been thought by some observers to mean that the mediastinal growth was primary and in some way incited the production of the leukemia, as Sternberg assumed in his hypothesis of the neoplastic nature of 'leukosarcoma.' The abruptness with which the blood picture may change from normal to leukemic is illustrated in the case reported by Borchardt. In this patient a blood count of 14,000, with 93% polymorphonuclears, had changed in two days to 91,800, with 94% lymphocytes. In one of the children whose case is here reported (case 4) the leukocytes were 21,500, with 72% polymorphonuclears, and a week later 140,000, with 11% polymorphonuclears and the remainder nongranular lymphocytes, but in none of the other patients were the counts made at sufficiently short intervals to detect a sudden alteration in the blood picture. . . . Probably the most interesting feature of leukemic mediastinal tumors lies in speculation about their origin, whether they are true neoplastic tumors or 'leukosarcomas' with unrestrained local cellular proliferation and secondary metastatic manifestations, or whether they consist essentially of extensive local infiltrations and accumulations of abnormal cells originating elsewhere and deposited in the mediastinum from the blood stream because of some chemotactic influence. Those who favor the neoplasm hypothesis can cite the observation of the instances in which the tumor has reached a considerable size before the abnormal cells appear in the blood; the presence of numerous cellular mitoses in the tumor, as in sarcomas; the tendency of the cells to spread beyond the original capsule of connective tissue and into the surrounding fat, and the similarity of these characteristics to those of sarcomatous growths. On the other hand, those who do not believe in the neoplastic origin of acute leukemia feel that the foregoing features may be explained on another basis; that one of the characteristics of the disease is the presence of infiltrations of the leukemic cells in such parenchymatous organs as the liver and the kidneys in addition to the spleen and lymphatic tissues, and that the local tumor masses in the mediastinum and elsewhere are manifestations of a similar infiltra-

tion. A study of the clinical and pathologic characteristics of this series of cases has left the impression that the latter hypothesis is the more plausible."

Ewing[5] was of the opinion that the mediastinal Hodgkin's disease of a number of writers was a thymic tumor. He re-examined a case reported by Symmers and found in it all the features of thymoma, including Hassall's corpuscles, polyhedral reticulum cells and myeloid giant cells.

He cited also a case of thymoma in a 19 year old woman which started clinically as a swelling in the left side of the neck which, after reaching the size of an egg, largely regressed, but soon recurred and the whole right side of the neck from ear to shoulder became swollen. The relation of the regression of the swelling to the menstrual cycle was not stated.

Major[13] reported a case of a thymus tumor associated with acute lymphatic leukemia in which the microscopic examination "suggests very strongly that we are dealing with a persistent thymus which has undergone a marked hyperplasia followed later by an extensive degeneration. The marked deformity of the sternum, consisting of a bowing outward with a large deep depression on the under surface corresponding to the thymus, indicated that the enlarged thymus had been present before the onset of the acute lymphatic leukemia."

Bichel[54] reported that: "The combination of tumor in the anterior portion of the mediastinum with a leukemic blood picture is relatively frequent. Among 217 patients with leukosis treated at the Radium Center for Jutland, in Aarhus, it was found in 4 cases. . . . It is oftenest found in children, chiefly in boys." Of these 217 cases, 22 were acute and all four of the "tumor cases" were in this group. It is interesting, too, that the mass was discovered chiefly in children where a more limited thoracic volume would predispose to an early display of symptoms attributable to it. Quoting Bichel, "When the patient enters the hospital, it will therefore oftenest be the mediastinal tumor that dominates the picture, and only after the latter has disappeared, or, at any rate, has diminished considerably, and the patient to all appearances has improved considerably and often has become entirely symptom-free, do the symptoms of acute leukosis develop and speedily lead to the fatal issue. . . . The hematologic features are very interesting, but are not yet fully elucidated. There is hardly any doubt, though, that quite a number of cases have been observed in which the blood picture in the beginning was perfectly normal, but later became acute leukemic—remarkably often in direct sequel to the irradiation therapy." Bichel's cases, as Cooke's and others, were very radiosensitive.

Mention should be made of the roentgen irradiation of the thymic tumors and the roentgenographic appearance of the thymus as a criterion for judging its size. First, Hammar[4] noted the rapid disintegration of the thymic lymphocytes after roentgen irradiation and the greater resistance of the reticular cells. He noted also the reconstruction of the organ in the course of time. Cooke[53] cited six cases from the literature where irradiation to the mediastinal mass was employed before the blood picture was leukemic. Five showed a prompt disappearance of the tumor but it recurred in two. In one instance the roentgen therapy apparently precipitated the acute leukemic manifestations but the patient had received an unusually large amount of irradiation. "In the others, the interval after irradiation before blood changes appeared was four months in three, three months in two, six weeks in three and two weeks in one. After the leukemic picture had appeared, death followed in from a few weeks to two months." Four of Cooke's children were treated by roentgen ray in the "preleukemic" period and all showed "remarkable clinical improve-

ment. . . . The irradiation was usually followed by a fall in the leukocyte count, with no significant change in the differential ratio. In two children with enlarged cervical lymph nodes the irradiation produced a rapid disappearance of these as well as of the mediastinal mass. Since the lymph nodes were not in the area directly irradiated, it seems likely that at least a part of the effect of the roentgen rays on these 'preleukemic' tumors is due to the irradiation of the blood." Decreased output of cells from the thymus may be another explanation. It may not be possible to destroy the medullary cells by irradiation without severely damaging the surrounding tissues. Perhaps the simplest way to eliminate this organ in cases where it is large would be to give just sufficient irradiation to diminish its mass and then to do a suprasternal thymectomy. The possibility of cervical thymus tissue should not be forgotten.

Second, Freeman[55] cited the work of Liss at the New York Nursery and Child's Hospital on the appearance of the thymus in infants. He took roentgenograms of 119 infants just after birth and of these found a large thymic shadow in 50, a small thymic shadow in 34 and no thymic shadow in 35. In the cases that came to autopsy, the size of the thymus as shown by roentgenogram compared very well with that found at post mortem. However, in two cases where there was no suggestion of a large thymus by roentgenogram, a large one was found overlying the heart. This makes it much more readily understandable how a large thymus could easily escape roentgenologic detection in the adult.

One should also keep in mind the fact that the authors quoted so freely did not consider very seriously the possibility that the thymus might, in some cases, put its cells into the circulation as fast as they were being produced and, therefore, remain "atrophic." The "infiltrating cells" were not readily conceived of as being emigrants from the thymus.

It would seem that the sequence of events may be as follows:

1. A mediastinal tumor (thymus) arises and may or may not cause pressure symptoms before a leukemic blood picture is evident.

2. The thymus releases its cells in huge numbers and this is reflected in the peripheral blood, with a concomitant involution of the thymus and an infiltration of its septa and the surrounding tissues with the emigrating cells.

3. Other tissues and organs are invaded and show the same infiltrative picture as the thymus. While these cells may settle in these other tissues and multiply, they are, in the first instance, immigrants.

4. Following partial or nearly complete distribution of its cells and the production of a leukemic picture elsewhere, the thymus may reconstitute itself in bulk and present the original picture of infiltration with leukocytes at the same time that the blood is characteristic of leukemia and other organs show the same apparent changes.

5. The possible independent origin in the other hemopoietic tissues must also be considered since after thymectomy in a high leukemia strain of mice (to be discussed later) there were still about 10% of the animals that developed leukemia. We must consider here, however, that (a) there may have been "regeneration" of small bits of thymus left at operation and (b) thymectomy was performed after potentially malignant cells had been seeded into the blood stream to settle elsewhere and reproduce themselves.

The onset of leukemia may be due to (1) a primary malignancy of the thymic cells and/or (2) a deficiency of adrenal and other hormonal factors necessary for the distribution, maturation and normal utilization of these cells, with their subsequent accumulation and reproduction.

EXPERIMENTAL CONSIDERATIONS IN LEUKEMIA

The foregoing statements have dealt solely with clinical and pathologic examinations on humans. In addition, there is clear experimental evidence showing the close relation between the thymus and leukemia. Gardner, Dougherty and Williams[56] studied lymphoid tumors in mice receiving steroid hormones and found that "approximately 80% of the lymphomas involved the thymus, spleen, liver, lymph nodes or other tissues. In approximately 20% the thymus and adjacent tissues alone were involved. The tumors grew when transplanted into mice of the same strain." Cramer,[57] referring to estrogens, stated: "It has been demonstrated experimentally for organs such as the mamma, the uterus and the thymus, that substances formed in the body and having hormonal functions may be carcinogenic for these organs." McEndy, Boon and Furth,[58] using a high-leukemia stock of mice (AK), noted that the thymus was almost always involved in leukemia affecting their animals, that "it is sometimes the sole organ involved, while the degree of leukemic infiltration in spleen and lymph nodes is variable and the bone marrow often appears normal." They concluded: "Thus the thymus may be the most common site of potentially neoplastic lymphocytes and consequently it seemed advisable to ascertain what effect its removal at an early age would have on the incidence of leukemia." They found that removal of the thymus at 31 to 71 days of age resulted in a reduction of the incidence of spontaneous leukemia from 77 to 8% in females and from 61 to 11% in males. Never had such low figures been observed in normal mice of that stock; the only comparable results were in a series of mice that were underfed and the question arose as to whether the effects of thymectomy were due to malnutrition. The authors were well aware that underfeeding causes an involution of the thymus and "It is thus conceivable that the decrease in the incidence of lymphoid neoplasms resulting from underfeeding is indirect and is the immediate consequence of involution of the thymus. However, neoplasms other than lymphomatosis are likewise infrequent among the underfed animals and if the effects of underfeeding are related to atrophy of the thymus it must be supposed that this organ contains substances that influence neoplastic tendencies in general.* Thus there are at least three possibilities to explain the results of thymectomy: (a) removal of sites of origin of leukemia, (b) developmental disturbance not specifically due to absence of thymus, (c) lack of hypothetical thymic hormones. The last assumption seems unlikely, since the administration of estrogen brings about an increased incidence of leukemia with involution of the thymus. An interpretation of the consequences of thymectomy, here described, must therefore be postponed until data are forthcoming from experiments such as that on the effect of thymic extract in normal and thymectomized animals." They noted also that splenectomy had no significant effect on the incidence of leukemia or on the longevity of the animals whereas a larger proportion of thymectomized animals reached an old age than among the controls as was also true for the underfed animals. Saxton, Boon and Furth[59] reported further observations on the effects of underfeeding in the same (AK) strain of mice. They noted also a low leukemic incidence (about 55%) in animals with infections, particularly pneumonia. In addition, "as concerns the sites of malignant transformation, bioassays thus far have yielded only fragmentary data. When the inoculations were successful, 'takes' were usually scored with several organs, namely lymph nodes, spleen and thymus. It follows that if leukemia is unicentric in origin the malignant cells

* The thymus is extremely rich in nucleoproteins. V.P.S.

soon find their way into the circulation and spread to and proliferate in numerous organs." These authors noted also an underdevelopment of spleen and lymphoid tissues as well as thymus of underfed mice. They concluded: "The incidence of spontaneous lymphoid leukemia in a high leukemia strain of mice was 65.0% in 100 normally fed control mice. In 79 related mice that received limited amounts of an otherwise adequate diet the incidence was 10.1%. The length of life of these mice was considerably prolonged by underfeeding." Furth[60] presented another paper on the prolongation of life with prevention of leukemia by thymectomy in mice, in which it was stated that, "These studies can serve as a model whereby the body benefits by removal of a useless organ which appeared innocuous until analyzed. While these observations are not directly applicable to any known situation in man it deserves emphasis that many neoplasms in human beings arise in organs that have survived their usefulness (e.g., uterus or breast), or in tissue rests which have not served any purpose. Removal of such organs would remove the potential menace from a neoplasm but because of the small liability of an individual to develop a neoplasm of a given organ, such procedures are not feasible. However, it is conceivable to neutralize all proliferative activity in some organ with no harm to the host. Using the thymus as a model, such experiments are in progress." It is stated in the summary: "Experiments here reported indicate that antecedent thymectomy does not influence the induction of cutaneous or lung tumors by methylcholanthrene while causing a reduction in the incidence of leukemia inducible by this hydrocarbon."

Law and Speirs[61] reported that in the RIL strain of mice, in which 80% develop spontaneous leukemia, "The majority of these leukemias involve initially and principally the thymus. The first symptom observed is usually that of dyspnea and the animals are at this time in the terminal stage of the disease." After treating these mice with injections of adrenal cortical extracts, "definite weight decreases of thymus, spleen and subcutaneous lymph nodes of treated leukemic mice were obtained. The effect on thymic mass was most severe resulting in a mean weight of 270 plus or minus 90 mg. in the experimental series compared with 663 plus or minus 66.5 mg. in leukemic controls."

Engelbreth-Holm and Rask-Nielsen[62] reported that: "It appears from the experiments . . . that injection of 0.02 mgm. of 9,10-dimethyl-1,2-benzanthracene in paraffin into mice of Street strain was followed by the development of leukemic tumors of the thymus only, apart from a single case of pulmonary adenoma. . . . The thymus is considerably more susceptible to carcinogenic action than the other tissues investigated."

Kaplan[63] reported that in radiation-induced lymphoid tumors of mice "the thymus is by far the organ most commonly involved. The spleen is distinctly less often infiltrated, and certain non-lymphoid organs (the lung, liver, kidney, heart and adrenal, in order of frequency) are invaded more often than the superficial lymph nodes. The tumors are lymphocytic lymphomas which, in most instances, appear to arise in the thymus, to disseminate to the spleen, lungs, liver, kidneys, and lymph nodes, and to cause leukemia in a considerable percentage of animals." In 1948, he presented another paper[64] on C57 black mice, stating: "Confirming the author's previous incidental observations, these results clearly establish the fact that lymphoid tumors developing in irradiated young mice of this strain regularly make their first appearance in the thymus gland. Their dissemination is a secondary phenomenon, with direct extension to the adjacent mediastinal soft tissues and to the lungs usually preceding histologic involvement of distant lymphoid structures."

SUMMARY

Careful research by numerous investigators has shown the thymus to be a producer of lymphocytes and myelocytes (and possibly also erythrocytes) which reach the circulation via the veins and lymphatics. It is therefore no longer necessary to consider the thymus as an enigmatic organ—an organ of unknown function—when its hematopoietic role is apparent. Likewise, it is sheer folly to go on believing that the thymus is merely an organ of infancy and childhood after it has been pointed out repeatedly by numerous workers in the field that this view is incorrect. One must have a moving dynamic concept of the organ as it is capable of swift and extensive changes in form and structure which take place under physiologic conditions chiefly by an unloading of its cortical cells into the vascular system and by the production of more to augment and replace them.

The thymus plays a far more important role in the genesis and perpetuation of leukemia than has hitherto been believed. The old but erroneous ideas about the immigration of cells into the thymus have led previous investigators astray in the interpretation of the histologic pictures presented in the thymus in both normal conditions and in leukemia. Leukocytes seen in the periphery of the lobules and in the interlobular septa have almost invariably been described as entering or "infiltrating" the thymus without any basis in fact; actually the cells are formed in the thymus and are migrating from it. The ultimate function of the thymus will not be clarified until the role of these leukocytes it produces—its chemical messengers—has been completely elucidated. However, clinical, pathologic and experimental data have been cited to support the thesis that leukemia may be primary in the thymus and a theory of the mode of genesis of leukemia has been suggested. A trial of thymectomy as a method of treatment of leukemia appears warranted.

References

1. Beard, J., Origin and histogenesis of thymus in Raja Batis, Zool. Jahrb. **17**:403, 1902.
2. Bell, E. T., Development of thymus, Am. J. Anat. **5**:29, 1905.
3. Badertscher, J. A., Development of thymus in pig. II. Histogenesis, Am. J. Anat. **17**:437, 1915.
4. Hammar, J. A., New views as to morphology of thymus gland and their bearing on problem of function of thymus, Endocrinol. **5**:543 and 731, 1921.
5. Ewing, J., Thymus and its tumors, Surg., Gynec. & Obst. **22**:461, 1916.
6. Harland, M., Early histogenesis of thymus in white rat, Anat. Rec. **77**:247, 1940.
7. Baillif, R. N., Response of thymic epithelial cells in induced involution, abstracted, Anat. Rec. **100**:6, 1948.
8. Murray, M. R., and Stout, A., Tissue cultures from human adult thymus glands, Anat. Rec. **100**:67, 1948.
9. Kindred, J. E., Quantitative study of hemopoietic organs of young albino rats, Am. J. Anat. **67**: 99, 1940.
10. Kindred, J. E., Quantitative study of hemopoietic organs of young adult albino rats, Am. J. Anat. **71**:207, 1942.
11. Andreasen, E., On lymphocytopoietic activity of different lymphoid organs of mice, abstracted, Anat. Rec. **100**:12, 1948.
12. Andreasen, E., Function of thymus: Critical remarks on theory and experiments of Bomskov, Acta Anat. **2**:275, 1947.
13. Major, R. H., Thymus tumor associated with acute lymphatic leukemia, Bull. Johns Hopkins Hosp. **29**:206, 1918.
14. Christensen, K., and Griffith, W. H., Involution and regeneration of thymus in rats fed choline deficient diets, Endocrinol. **30**:574, 1942.
15. Dudgeon, L. S., Contribution to pathology of thymus gland, J. Path. & Bact. **10**:173, 1904.
16. Renaut, J., Traité d'Histologie Pratique, Paris, Rueff et Cie, 1897, vol. 2, chap. 1, p. 566.

17. Severeaunu, G., Die Lymphgefässe der Thymus, Arch. f. Anat. u. Entwickl. (Leipsig), 1909, pp. 93-98.
18. Cowdry, E. V., Textbook of Histology, Philadelphia, Lea & Febiger, 1946.
19. Selye, H., Thymus and adrenals in response of organism to injuries and intoxications, Brit. J. Exper. Path. **17**:234, 1936.
20. Farris, E. J., Increase in lymphocytes in healthy persons under certain emotional states, Am. J. Anat. **63**:297, 1938.
21. Martin, H. E., Physiological leukocytosis, J. Physiol. **75**:113, 1932.
22. Garrey, W. E., and Bryan, W. R., Variations in white blood cell counts, Physiol. Rev. **15**:597, 1935.
23. Crotti, A., Diseases of Thyroid, Parathyroids and Thymus, Philadelphia, Lea & Febiger, 1938.
24. Paton, D. N., and Goodall, A., Contribution to physiology of thymus, J. Physiol. **31**:49, 1904.
25. Warfield, L. M., Differential leukocyte count in newborn, Am. Med. **4**:457, 1902.
26. Boyd, E., Growth of thymus, Am. J. Dis. Child. **33**:867, 1927.
27. Neste, Dr., Die Beziehungen des Status Thymico-lymphaticus zum Selbstmord von Soldaten, Arch. f. Psychiat. **60**:43, 1919.
28. Falta, W., Endocrine Diseases Including Their Diagnosis and Treatment, Philadelphia, P. Blakiston's Son & Company, 1923.
29. Richter, M., Die "Hyperplasie" des lymphatischen Apparates Bei Kriegsteilnehmern, München. med. Wchnschr. **66**:890, 1919.
30. Park, E. A., and McClure, R. D., Results of thymus extirpation in dog, Am. J. Dis. Child. **18**: 317, 1919.
31. Farris, E. J., and Yeakle, E. H., Persistence of thymus remnant in aged rats, abstracted, Anat. Rec. **89**:572, 1944.
32. Fenger, F., On size and composition of thymus gland, J. Biol. Chem. **20**:115, 1915.
33. Bürker, D., Blut und Lymph, in Handbuch der normalen und pathologischen Physiologie, edited by A. Bethe and others, Berlin, Julius Springer, 1928.
34. Hammett, F. S., Studies on thyroid apparatus. XXXVII. Role of thyroid apparatus in growth of thymus, Endocrinol. **10**:370, 1926.
35. Hammar, J. A., On asserted non-existence of age involution of thymus gland, Endocrinol. **11**:18, 1927.
36. Smith, C., and Wilson, C. E., Thymus in mice fed choline deficient diets, abstracted. Anat. Rec. **100**:124, 1948.
37. Morgulis, S., Fasting and Undernutrition, New York, E. P. Dutton & Co., Inc., 1923.
38. Jonson, A., Studien über die Thymusinvolution. Die akzidentelle Involution be Hunger, Arch. f. mikr. Anat. **73**:390, 1909.
39. Andersen, Dorothy H., Effect of food and of exhaustion on pituitary, thyroid, adrenal and thymus glands of rat, J. Physiol. **85**:162, 1935.
40. Ingle, D. J., Problems relating to adrenal cortex, Endocrinol. **31**:419, 1942.
41. Dontigny, P., Morphologic effect of desoxycorticosterone acetate on thymus, Proc. Soc. Exper. Biol. & Med. **63**:248, 1946.
42. Marine, D., Present status of functions of thyroid gland, Physiol. Rev. **2**:521, 1922.
43. Marine, D., Thyroid, parathyroids and thymus, in Special Cytology, edited by E. V. Cowdry, New York, Paul B. Hoeber, Inc., 1928, vol. 1.
44. Evans, H. M., and Simpson, M. E., Reduction of thymus by gonadotropic hormone, Anat. Rec. **60**:423, 1934.
45. Henderson, J., On relationship of thymus to sexual organs, J. Physiol. **31**:222, 1904.
46. Moore, R. A., Textbook of Pathology, Philadelphia, W. B. Saunders Company, 1945, p. 1032.
47. Craver, L. F., and MacComb, W. S., Lymphatic leukemia with thymic enlargement: Brief review of literature with case reports, Am. J. Cancer **16**:277, 1932.
48. Crosby, E. H., Malignant tumors of thymus gland, Am. J. Cancer **16**:461, 1932.
49. Evans, W. A., and Leucutia, T., Neoplastic nature of lymphatic leucemia and its relation to lymphosarcoma, Am. J. Roentgenol. **15**:497, 1926.
50. Thorpe, E., Unusual case of thymic hypertrophy, Arch. Pediat. **44**:126, 1927.
51. Scott, A. J., Lymphosarcoma of mediastinum in child, Arch. Pediat. **44**:548, 1927.

52. Margolis, H. M., Thymus gland in lymphatic leukemia: Its bearing on histogenesis of small thymic cells, Arch. Path. **9**:1015, 1930.
53. Cooke, J. V., Mediastinal tumor in acute leukemia: Clinical and roentgenologic study, Am. J. Dis. Child. **44**:1153, 1932.
54. Bichel, J., Mediastinal tumors in leukosis, Acta radiol. **28**:81, 1947.
55. Freeman, R. G., Symptoms and treatment of thymus hypertrophy in infancy, Tr. Am. Pediat. Soc. **35**:116, 1923.
56. Gardner, W. T., Dougherty, T. F., and Williams, W. L., Lymphoid tumors in mice receiving steroid hormones, Cancer Research **4**:73, 1944.
57. Cramer, W., Origin of cancer in man, J.A.M.A. **119**:309, 1942.
58. McEndy, D. P., Boon, M. C., and Furth, J., On role of thymus, spleen, and gonads in development of leukemia in high-leukemia stock of mice, Cancer Research **4**:377, 1944.
59. Saxton, J. A., Boon, M. C., and Furth, J., Observations on inhibition of development of spontaneous leukemia in mice by underfeeding, Cancer Research **4**:401, 1944.
60. Furth, J., Prolongation of life with prevention of leukemia by thymectomy in mice, J. Gerontol. **1**:46, 1946.
61. Law, L. W., and Speirs, R., Response of spontaneous lymphoid leukemias in mice to injection of adrenal cortical extracts, Proc. Soc. Exper. Biol. & Med. **66**:226, 1947.
62. Engelbreth-Holm, J., and Rask-Nielsen, R., On sensitivity of different tissues in street strain mice to 9,10-dimethyl-1,2-benzanthracene, Cancer Research **7**:129, 1947.
63. Kaplan, H. S., Observations on radiation-induced lymphoid tumors of mice, Cancer Research **7**:141, 1947.
64. Kaplan, H. S., Comparative susceptibility of lymphoid tissues of strain C57 black mice to induction of lymphoid tumors by irradiation, J. Nat. Cancer Inst. **8**:191, 1948.

7930 Gridley Avenue

NEWS AND ANNOUNCEMENTS

The University of Minnesota announces a continuation course in pediatrics on April 10-12, 1950. This course, which will be presented at the Center for Continuation Study, is intended for physicians specializing in pediatrics and will be devoted to disorders of metabolism and endocrine function. Distinguished visiting physicians who will participate as faculty members for the course are Dr. Daniel C. Darrow, Yale University School of Medicine, New Haven, Conn., and Dr. George M. Guest, Children's Hospital, Cincinnati, Ohio.

* * *

Dr. John P. Hubbard has been appointed George S. Pepper Professor of Public Health and Preventive Medicine and Chairman of the Department of Public Health and Preventive Medicine at the University of Pennsylvania School of Medicine. His appointment is part of an expanding program of teaching and service in the field of preventive medicine at the University of Pennsylvania. Special emphasis is being laid on industrial medicine and on maternal and child health.

Dr. Hubbard has also been appointed Executive Director of the National Board of Medical Examiners.

* * *

The American Academy of Pediatrics announces that the State Chairman from Illinois has been changed from Dr. Eugene T. McEnery to Dr. John L. Reichert.

* * *

Dr. Roy M. Greenthal, aged 54, well-known Milwaukee pediatrician, died Jan. 27, 1950, after a short illness.

Dr. Greenthal was the discoverer of the stain for making smears of diphtheria bacilli which now bears his name. He also was instrumental in the formulation of lactic acid milk for feeding infants.

He received his medical degree from the University of Michigan in 1918 and interned at the New York Nursery and Child's Hospital, Mt. Sinai Hospital in New York and in Boston hospitals. The University of Michigan Medical school gave him an instructor's post in pediatrics from 1920 to 1922. After 1922 Dr. Greenthal practiced continually in Milwaukee.

ERRATUM

The footnote on p. 237, vol. 5, February 1950 issue, indicated that product II is at present being manufactured with a calcium:phosphorus ratio of 1.0 as a result of the addition of phosphoric acid commonly used in milk processing. This is in error. Since October 1948, product II has been manufactured with a standardized calcium:phosphorus ratio of 1.5 and no phosphoric acid is used. The research reported in this paper, however, was conducted on the product of prior manufacture which contained a calcium:phosphorus ratio of 1.0.

BOOK REVIEWS

Essentials of Adoption Law and Procedure, Publication no. 331, Children's Bureau, Federal Security Agency, Washington, D.C., Government Printing Office, 1949.

This publication is a revision of a preliminary draft issued in December 1944. The revision is a result of suggestions received from many agencies after study of the preliminary draft, of a conference with an advisory group representing both public and private agencies from a number of States and of further consideration by the Children's Bureau.

This material was prepared with the hope that it will be helpful to the many groups interested in adoption legislation and that it will be of service in protecting children who need permanent foster homes.

Single copies are available without charge from the Children's Bureau, FSA, Washington 25, D.C. Copies may also be purchased from the Superintendent of Documents, Government Printing Office, Washington 25, D.C.

Die Tuberkulose des Kindes, Heinrich Brugger, M.D., Reiner W. Muller, M.D., and Maria Birkenfeld, M.D., New York, Grune & Stratton, 1948, $5.00, 340 pp.

The authors emphasize in the foreword that any textbook on children's tuberculosis should describe the morbid symptoms of the total organism, not only the specific reactions of single tissues and organs. They follow this sound principle of didactic presentation in the main 3 sections: endothoracic tuberculosis, tuberculosis of bones and muscles and tuberculosis of the skin. Numerous case reports describe in detail changes such as type of atelectasis, shadows of paratracheal glands and diagnostic signs of interlobar pleurisy. In each of these case presentations, the previous history, the laboratory findings, the later courses of the disease and constitutional factors are likewise considered. The section on endothoracic tuberculosis deserves special mention as a very good source of information. Single chapters discuss such subjects as structure and signs of primary lesions, variability of bronchial tuberculosis, quiescent and inflammatory types of atelectasis and acute and protracted miliary tuberculosis. The chapter on the relation between miliary tuberculosis and tuberculous meningitis is most instructive. Some of the film reproductions are informative, others do not show what the text indicates, e.g., bronchogenic dissemination or small cavities. The chapter on differential diagnosis is useful. It is a complete presentation of the subject, well illustrated by personal experiences. The only omission is histoplasmosis, unknown to the German observers, who confessed in their preface that they could not consider the foreign literature after 1939.

This is a great disadvantage. BCG, streptomycin, bronchoscopic methods are hardly mentioned. Procedures that are only of historical interest (Ponndorf, Petruschky) are too meticulously discussed. However, sound clinical observations never become obsolete. The tuberculosis sanitarium in Wangen has been one of the leading European institutions for the past decades and the enormous increase of tuberculosis in Germany even before 1945 has offered unusual opportunities for the clinical observer.

Therefore, this textbook can be recommended though many therapeutic methods are not up-to-date.

Epilepsy and Convulsive Disorders in Children, Edward M. Bridge, M.D., New York, McGraw-Hill Company, 1949, $8.50, 670 pp.

In 1927, a special clinic was organized at the Johns Hopkins Hospital to care for children with epilepsy. This book, in part, summarizes the wealth of material obtained by the careful analysis of the records of more than 700 patients treated at the clinic since its opening. The discussion of the overall problem of epilepsy in children is based primarily on the results of this study with a judicious integration of the pertinent literature. The result is an excellently written, well planned and comprehensive presentation of the problem.

The importance of psychogenic factors in the etiology, treatment and prognosis of convulsive disorders in children has been stressed with increasing frequency and force during the last few years. However, the understanding and practical competency with which it is handled by Dr.

Bridge is excelled nowhere else and represents, in this reviewer's opinion, the most valuable aspect of the book. The detailed presentation of advice to be given the family and child and the varied community and school responsibilities in the care of the epileptic child is a welcome departure from the brief and superficial handling usually accorded this aspect of the problem.

The discussion of etiologic factors, both internal and environmental, is complete and adequately presented. Also commendable are the chapters on general management, psychotherapy, prognosis and diagnostic procedures.

The only serious criticism which may be raised is that relating to drug therapy which does not receive the detailed and meticulous discussion so apparent elsewhere in the book.

CHANGING DISCIPLINES, John A. Ryle, M.D., New York, Oxford University Press, 1948, $3.75, 122 pp.

In order to appreciate this excellent little book of 6 lectures, one should know something of the author. Dr. John A. Ryle, during 30 years in clinical medicine, became one of the leading internists in Britain. Then, he resigned the Regius Professorship of Physics at the University of Cambridge to become Professor of Social Medicine in the University of Oxford and Director of the first Institute of Social Medicine. These lectures present the philosophy and the thinking which led him to give up an assured career in clinical medicine to pioneer in this new field.

Dr. Ryle contrasts the study of a disease in the individual, which requires the cooperative effort of various specialist physicians, laboratory workers and others, with the study of group diseases, which calls for the teamwork of the physician, the epidemiologist, the statistician, the social workers and others. He argues that modern medical specialization and teaching has concentrated on individual pathology, with little emphasis on the social conditions underlying many of these illnesses, little discussion of prevention and very little concern for the problems of the "well" patient. He points out that cholera, malaria, the dysenteries and hookworm are all social diseases and are preventable. Similarly he believes that peptic ulcer, the neuroses and accidental injuries have social aetiologies which are susceptible of study and of prevention.

He presents material on the incidence of angina pectoris, coronary artery disease, tuberculosis and peptic ulcer according to the 5 socio-economic categories used in the Registrar General's Office and suggests study of the implications of this data.

The teaching and research in the new Institute of Social Medicine at Oxford is described. One chapter is devoted to problems in the measurement of health which discusses some of the recent work in this area and emphasizes the need for more data about the "normal" person and the range and variability of normal. The final lecture is a discussion of "medical ethics and the new humanism."

CARDIOPATÍAS CONGÉNITAS DE LA INFANCIA, Prof. Agustín Castellanos, Havana, M. V. Fresneda, 1948, $9.00, 406 pp.

The presentation of subjects is excellent; its organization is logical and its description is clear. The content is rich and interesting and well synthesized in such a manner that it is presented with clarity and is easily comprehended.

The book presents a good study of the embryologic development of the heart, and an extensive description of the most common congenital dystrophies, their signs and symptoms and discussion of the investigation of the diagnostic procedures, giving also to surgery an important role in the treatment of some of these congenital anomalies. The book is well illustrated by anatomic drawings and photographs of chest roentgenograms, as well as angiocardiograms. The book is highly recommended as a comprehensive guide in the field of cardiac anomalies for medical students, general practitioners interested in advanced study of this subject and particularly to the pediatrician who has the first opportunity to deal with early manifestations of such pathologic entities in infants.

There is a careful résumé, closing each major section, which will be appreciated by readers who have a limited use of Spanish. There is a comprehensive bibliography of 8 pages and an atlas of 20 diagrams, illustrating roentgenograms arranged on dextro and levo pages.